Tetrahedron Letters, Vol. 22, No. 15, pp 1437 - 1440,1981
Printed in Great Britain

0040-4039/81/151437-04$02.00/0

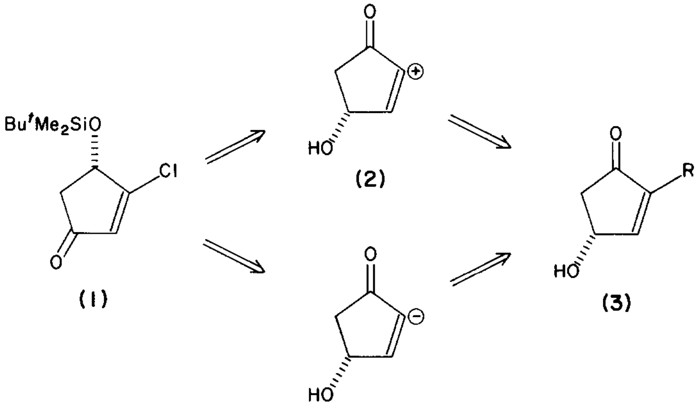
CYCLOPENTANOIDS FROM PHENOL. PART VII.[1] PREPARATION AND REACTIONS OF A 3-HYDROXY-5-OXOCYCLOPENT-1-ENYL CARBANION EQUIVALENT

Melvyn Gill, H. Paul Bainton, and Rodney W. Rickards*

Research School of Chemistry, Australian National University
Canberra, A.C.T. 2600, Australia

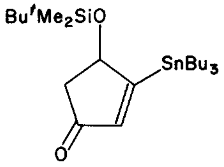
Summary: $(3S^*,5R^*)$-1-Lithio-5-(*t*-butyldimethylsilyloxy)-3-(tetrahydropyran-2-yloxy)cyclopent-1-ene (7) is prepared from phenol *via* the chlorocyclopentenone (1) and the stannylcyclopentenediol derivative (6); this latent 3-hydroxy-5-oxocyclopent-1-enyl carbanion (7) reacts efficiently with various electrophiles to form substituted cyclopentenediol derivatives (8) which can be converted into the corresponding 2-substituted 4-hydroxycyclopent-2-enones (9).

We have previously described the conversion of both racemic and optically pure 4-(*t*-butyldimethylsilyloxy)-3-chlorocyclopent-2-enone (1) into the corresponding 2-alkyl-4-hydroxycyclopent-2-enones (3) by conjugate addition-elimination of an organometallic reagent followed by transposition of ring oxygen functions.[1-4] In this process the chlorocyclopentenone (1) is synthetically equivalent to the 3-hydroxy-5-oxocyclopent-1-enyl carbocation (2) which undergoes nucleophilic alkylation. We report now a complementary process based upon the same chlorocyclopentenone (1) which involves the electrophilic substitution of a synthetic equivalent of the 3-hydroxy-5-oxocyclopent-1-enyl carbanion (4).

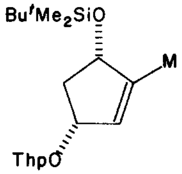


The racemic chlorocyclopentenone (1) is readily available in four steps from phenol.[3] Addition of this substrate (in THF) to lithium bis(tributylstannyl)cuprate

(1.1 equiv., prepared at -25° from tributylstannyl-lithium[5] and cuprous bromide-dimethylsulphide[6]) in THF-Me$_2$S at -25° gave the stannylcyclopentenone (5)[7] in 84% yield,[8] ^{1}H n.m.r.(CDCl$_3$)δ 0.10 and 0.12 (each 3H, s, SiMe$_2$), 0.90 (9H, s, Bu^t), 0.80-1.80 (27H, m, Bu), 2.15 (1H, dd, *J* 18 and 3Hz, H-5 *trans* to H-4), 2.67 (1H, dd, *J* 18 and 6Hz, H-5 *cis* to H-4), 4.99 (1H, ddd, *J* 6, 3 and 1Hz, H-4), and 6.30 (1H, d, *J* 1Hz, H-2). Stereospecific reduction[4] of the carbonyl group in compound (5) with lithium tri-*s*-butylborohydride (THF, -78°) followed by tetrahydropyranylation of the newly-formed hydroxy group gave the (1*R**,4*S**)-stannylcyclopentenediol derivative (6) in 94% overall yield from the stannylcyclopentenone (5), ^{1}H n.m.r.(CDCl$_3$)δ 0.08 (6H, s, SiMe$_2$), 0.90 (9H, s, Bu^t), 0.82-1.92 (34H, m, Bu , CH$_2$ in Thp ring and H-5 *trans* to H-1 and H-4), 2.67 and 2.69 (each 0.5H, dt, *J* 13.0 and 6.5Hz, H-5 *cis* to H-1 and H-4 in each diastereoisomer), 3.51 and 3.93 (each 1H, m, CH$_2$O), 4.67 (3H, m, H-1, H-4 and OCHO), and 6.00 (1H, m, H-3).

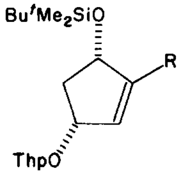


(5)

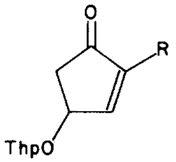


(6) M = SnBu$_3$

(7) M = Li



(8)



(9)

At -78° tin-lithium exchange[9] between the stannylcyclopentene (6) and butyl-lithium (1.1 equiv., THF) proved prohibitively slow as monitored by the chromatographic appearance of the destannylated cyclopentene (8; R=H). However, with butyl-lithium (2 equiv.) at -45° transmetalation was complete within 0.75h, whereupon quenching with D$_2$O afforded the 2-deuteriocyclopentene (8; R=D) containing >95 atom % excess of D (mass spectrometry). The intermediate 1-lithio-5-(*t*-butyldimethylsilyloxy)-3-(tetrahydropyran-2-yloxy)cyclopent-1-ene (7), generated at -45° and subsequently chilled to -78°, reacted efficiently with a variety of other electrophiles to yield the substituted cyclopentenediol derivatives (8) shown in the Table.

Selective removal of the silyl protecting group in the methylated cyclopentene (8; R=Me) with non-aqueous fluoride ion, followed by oxidation of the newly-liberated hydroxy function with pyridinium chlorochromate, gave the 2-methyl-4-hydroxycyclopent-2-enone (9; R=Me) as a mixture of diastereoisomers in 88% yield over the two steps, ^{1}H n.m.r. (CDCl$_3$)δ 1.4-1.9 (6H, m, CH$_2$), 1.80 (3H, m, Me), 2.29 and 2.24 (each 0.5H, dd, *J* 18.5 and 2.5Hz, H-5 *trans* to H-4), 2.73 and 2.80 (each 0.5H, dd, *J* 18.5 and 6.0Hz, H-5 *cis* to H-4), 3.56 and 3.90 (each 1H, m, CH$_2$O), 4.82 (2H, m, H-4 and OCHO), 7.22 (1H, m, H-3). The higher alkylated cyclopentene analogues (8; R=Bu) and (8; R=[CH$_2$]$_7$OSiBu^{t}Me$_2$) were identical with the compounds prepared previously from the chlorocyclopentenone (1) by the conjugate addition-elimination route,[3,4] and have already been converted into the corresponding 2-alkyl-4-hydroxycyclopent-2-enones (9; R=Bu) and (9; R=$[CH_2]_7OSiBu^tMe_2$).[4] These interconversions illustrate the synthetic equivalence of the lithiocyclopentene (7) with the 3-hydroxy-5-oxocyclopentenyl carbanion (4).

Table. Reaction of Lithiocyclopentene (7) with Electrophiles

Electrophile	Product, R in (8)	Yield (%)[a]
$CH_2{=}CHCH_2Br$	$CH_2 = CHCH_2$	84
BuI[b]	Bu	28
MeI[b]	Me	77
$I[CH_2]_7OSiBu^tMe_2$[b]	$[CH_2]_7OSiBu^tMe_2$	30
$ClCO_2Et$	CO_2Et	100
HCO_2Me	CHO	79
Me_2CO	$C(OH)Me_2$	62
PhCHO	CH(OH)Ph	79
$ClCH_2OCH_2Ph$	CH_2OCH_2Ph	94

[a] Yields refer to isolated, purified material,[7] and were not optimised.

[b] Electrophile added at -45°.

This 3-hydroxy-5-oxocyclopentenyl carbanion equivalent (7)[10] complements our previous development of the corresponding carbocation equivalent (1)[3,4] and greatly extends the synthetic utility of such phenol-derived cyclopentanoids. For example, certain functionality such as -CHO, $-CO_2Me$, and $-CH_2OH$[11] can be efficiently introduced with electrophiles into the cyclopentenyl carbanion (7) which cannot readily be introduced with nucleophiles into the chlorocyclopentenone (1). Thus reaction of the latter compound (1) with various formyl carbanion equivalents such as the anions derived from 1,3-dithiane,[12] N,N-diethylaminoacetonitrile,[13] and benzothiazole[14] afforded kinetically-controlled 1,2-addition products which could not be induced to undergo rearrangement[15] to the desired 1,4-addition-elimination products. Furthermore, the chlorocyclopentenone (1) does not react with the cuprate derived from benzyloxymethyl-lithium, a hydroxymethyl carbanion equivalent.

Finally, the application of the present route to the enantiomerically pure chlorocyclopentenone (1)[1,2] affords ready access to the lithiocyclopentene (7), its substitution products (8), and the derived 2-alkyl-4-hydroxycyclopent-2-enones (9) in chiral form.

Acknowledgements

We thank Messrs A.J. Herlt and P.J. Green for skilful technical assistance in this project.

References and Notes

1. Part VI, M. Gill and R.W. Rickards, submitted to Aust. J. Chem.
2. M. Gill and R.W. Rickards, J.Chem.Soc., Chem. Commun., 121 (1979).
3. R.M. Christie, M. Gill, and R.W. Rickards, J.Chem.Soc., Perkin I, in press.
4. M. Gill and R.W. Rickards, J.Chem.Soc., Perkin I, in press.
5. W.C. Still, J.Am.Chem.Soc., **100**, 1481 (1978).
6. H.O. House, C.-Y. Chu, J.M. Wilkins, and M.J. Umen, J.Org.Chem., **40**, 1460 (1975).
7. Satisfactory elemental analyses and spectroscopic data have been obtained for all new compounds described herein.
8. Lower yields of (5) were obtained using lithium phenylthio(tributylstannyl)cuprate, *cf.* E. Piers and H.E. Morton, J.Chem.Soc., Chem. Commun., 1033 (1978), and J.Org.Chem., **44**, 3437 (1979).
9. S.-M.L. Chen, R.E. Schaub, and C.V. Grudzinskas, J.Org.Chem., **43**, 3450 (1978); P.W. Collins, C.J. Jung, A. Gasiecki, and R. Pappo, Tetrahedron Lett., 3187 (1978).
10. Appropriately protected lithiocyclopentenes of type (7) may also be regarded as latent 5-hydroxy-3-oxocyclopent-1-enyl and 3,5-dihydroxycyclopent-1-enyl carbanions. For an alternative equivalent to the latter carbanion, see D.A. Evans, T.C. Crawford, T.T. Fujimoto, and R.C. Thomas, J.Org.Chem., **39**, 3176 (1974).
11. For potential applications and alternative syntheses of 4-hydroxy-2-hydroxymethylcyclopent-2-enone see J.D. Elliott, M. Hetmanski, R.J. Stoodley, and M.N. Palfreyman, J.Chem.Soc., Chem. Commun., 924 (1980).
12. C.A. Brown and A. Yamaichi, J.Chem.Soc., Chem. Commun., 100 (1979).
13. G. Stork, A.A. Ozorio, and A.Y.W. Leong, Tetrahedron Lett., 5175 (1978).
14. E.J.Corey and D.L. Boger, Tetrahedron Lett., 5 (1978).
15. S.R. Wilson, R.N. Misra, and G.M. Georgiadis, J.Org.Chem., **45**, 2460 (1980).

(Received in UK 23 January 1981)