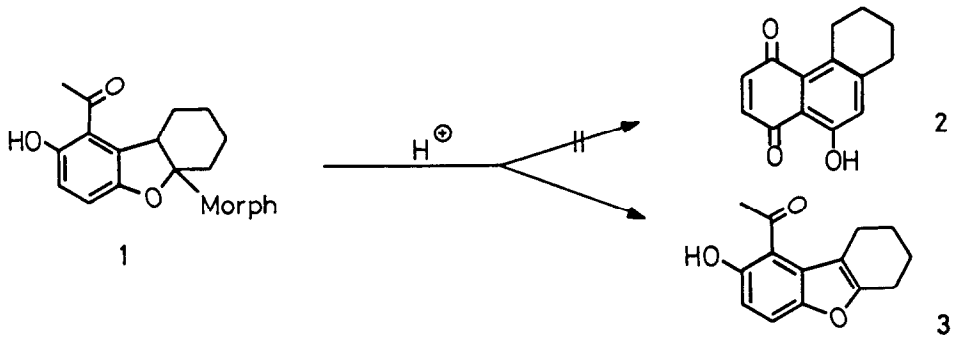
Tetrahedron Letters,Vol.26,No.51,pp 6281-6284,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

STUDIES ON QUINONES. XV[1]. A CONVENIENT ENTRY INTO THE TETRAHYDROPHENANTHRENE-1,4-QUINONE SYSTEM UTILIZING THE DIENONE-PHENOL REARRANGEMENT OF SPIRO [CYCLOPENTANENAPHTHALENE] TRIONES

R. Cassis, M. Scholz, R. Tapia and J.A. Valderrama*
Facultad de Química, Pontificia Universidad Católica de Chile. Casilla 6177, Santiago, Chile

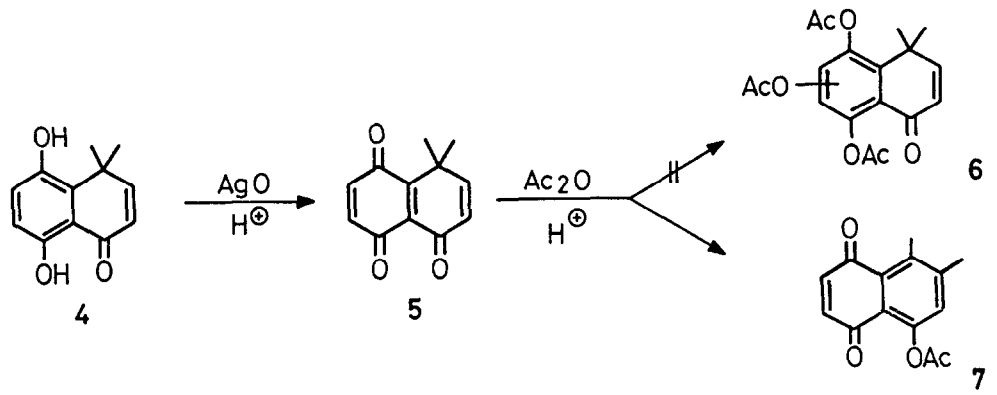
Abstract: A four-step approach to the synthesis of 10-acetyloxi-5,6,7,8-tetrahydrophenanthrene-1,4-derivatives, starting from acylbenzoquinones, is described.

Our interest in synthesis of angular tricyclic quinones as precursors of rabelomycin and related natural antibiotics[2] led us to investigate the chemistry of 4-acyl-2,3-dihydro-5-benzo[*b*]furanols which are easily prepared by reaction of acylbenzoquinones and enamines.[3-6] These studies revealed that the acid-catalysed rearrangement of the aforementioned heterocycles provides a route for the preparation of carbocyclic quinones and quinone precursors. Nevertheless, the lack of rearrangement of the cyclic O,N-ketal **1** which afforded the elimination product **3** in acid medium[6] frustrated our hopes of preparing 10-hydroxy-5,6,7,8-tetrahydrophenanthrene-1,4-dione **(2)** by this route.



In the present communication we report a preliminary study to synthesize 5,6,7,8-tetrahydrophenanthrene-1,4-diones derivatives by using 4-acyl-benzo[*b*]furans containing a spirocyclopentane substituent on C-3 position. Our basic strategy employs a sequence which involves two rearrangements to construct the angular tricyclic system.

In the course of modification studies of quinone **5** [m.p. 146-147°C; IR (KBr): 1690, 1665, 1650, 1620 cm^{-1}; ^{1}H-NMR (100 MHz, $CDCl_3$): δ 1.58 (s, 6H), 6.34 (d, 1H, J∿10Hz), 6.75 (s, 2H), 6.77 (d, 1H, J∿10Hz) ppm] obtained in 87% yield by oxidation of **4** with silver(II) oxide, the Thiele-Winter acetoxylation reaction[7] was attempted using standard methods (acetic anhydride containing concentrated sulphuric acid, room temperature). Interestingly, under these conditions, quinone **5** does not lead to the expected triacetate **6** but gives in high yield (83%) the dienone-phenol rearranged product **7**, m.p. 102-104°C; IR (KBr): 1760, 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ2.42 (s, 3H), 2.43 (s, 3H), 2.61 (s, 3H), 6,71 (d, 1H, J∿10Hz), 6.80 (d, 1H, J∿10Hz), 7.14 (s, 1H) ppm.

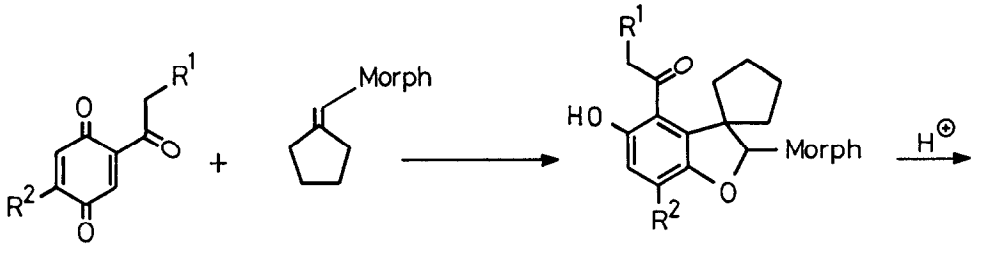


These findings[8] prompted us to explore a synthetic approach for building up 10-hydroxy-5,6,7,8-tetrahydrophenanthrene-1,4-dione derivatives. For this purpose we planned to make the spironaphthalenetrione **12a** which could then be converted by dienone-phenol rearrangement[9] into the angular tricyclic quinone **13a**.

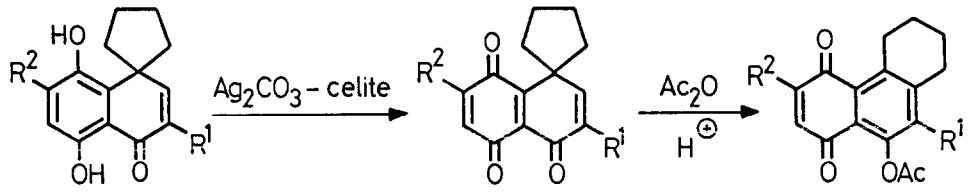
The preparation of the required naphthalentrione **12a** was initiated by addition of enamine **9**[10] to 2-acetyl-1,4-benzoquinone **(8a)**[11], resulting in the formation of cyclic O,N-acetal **10a** [73%; m.p. 169-170°C; IR (KBr): 3325, 1680 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 1.5-2.1 (m, 8H), 2.2-2.8 (m, 4H), 2.60 (s, 3H), 3.61 (t, 4H, J∿4Hz), 4.68 (s, 1H), 6.55 (d, 1H, J∿8Hz), 6.65 (d, 1H, J∿8Hz) ppm].

The rearrangement of **10a** in acid medium, according to the procedure previously described[6], afforded the spironaphthalenone **11a** [70%; m.p. 237-238; IR(KBr): 3180, 1650, 1620 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ1.4-2.3 (m, 8H), 6.18 (d, 1H, J∿10Hz), 6.72 (d, 1H, J∿9Hz), 7.10 (d, 1H, J∿10Hz), 7.19 (d, 1H, J∿9Hz), 9.39 (s, 1H), 12.56 (s, 1H) ppm], which was oxidized with silver carbonate-Celite reagent[12] to give quinone **12a** [90%; m.p. 126-128°C; IR(KBr): 1680, 1660, 1635, 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ1.6-2.5 (m, 8H); 6.28 (d, 1H, J∿10Hz), 6.76 (s, 2H), 6.95 (d, 1H, J∿10Hz) ppm].

Treatment of **12a** with acetic anhydride in the presence of a catalytic amount of concentrated sulphuric acid at room temperature gave 87% yield of the desired angular quinone **13a**, m.p. 120-122°C; IR (KBr): 1750, 1660, 1645 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ1.80 (m, 4H), 2.41 (s, 3H), 2.85 (m, 2H), 3.19 (m, 2H), 6.68 (d, 1H, J≈10Hz), 6.77 (d, 1H, J≈10Hz), 7.05 (s, 1H) ppm.



8a-c **9** **10a-c**



11a-c **12a-c** **13a-c**

	a	b	c
R^1	H	Me	H
R^2	H	H	Me

On the basis of these results we decided to apply the above synthetic sequence to the preparation of angular quinones **13b** and **13c**. The required cyclic O,N-acetals **10b** and **10c** were obtained (65 and 66%) by reaction of enamine **9** with 2-propanoyl and 2-acetyl-5-methyl-1,4-benzoquinone (**8b**, **8c**)[13,14].

Acid catalysed rearrangement of **10b** and **10c**, and subsequent treatment of intermediates **11b** and **11c** with silver carbonate-Celite reagent, afforded the corresponding quinones **12b** and **12c** in 62 and 64% overall yields. Finally, dienone-phenol rearrangement of the latter gave the angular quinones **13b** and **13c** in 82 and 80% yield respectively[15].

We believe that the synthetic procedure presented here does offer a simple and efficient route for preparation of C-10 oxygenated 5,6,7,8-tetrahydrophenanthrene-1,4-diones, which could serve as a useful method for the construction of biological active angular quinones.

Acknowledgement

This work was supported by a Research Grant (27/84) from the Pontificia Universidad Católica de Chile. We thank the Graduate Program (U.C.) for a pre-doctoral fellowship to R.C.

References and Notes

1. Part XIV of this series: B. Errazuriz, R. Tapia and J.A. Valderrama, Tetrahedron Lett., 26, 819 (1985).
2. a) W-C, Liu, W.L. Parker, D.S. Slugarchyk, G.L. Greenwood, S.F. Graham E. Meyers, J. Antibiotics, 23, 437 (1970); b) M. Sezaki, S. Kondo, K. Maeda, H. Umezawa and M. Ohno, Tetrahedron, 26, 5171 (1970); c) J. Bérdy, A. Aszalos, M. Bostian and K.L. Mc Nitt, "CRC Handbook of Antibiotic Compounds", Vol. III, Quinone and Similar Antibiotics, CRC Press, Inc., 1980, p 167 and references cited therein.
3. J.A. Valderrama and J.C. Vega, An. Quím., 73, 1212 (1973).
4. L. Barrios, V.M. Ruiz, R. Tapia, J. Valderrama and J.C. Vega, Chem. Lett., 187 (1980).
5. C.G. Castro, J.G. Santos, J.C. Valcárcel and J.A. Valderrama, J. Org. Chem., 48, 3026 (1983).
6. R. Cassis, R. Tapia and J.A. Valderrama, J. Heterocyclic Chem., 21, 869 (1984).
7. J.F.W. Mc Omie and J.M. Blatchly, Org. React., 19, 199 (1972).
8. Presented at the XIII Annual Chilean Meeting of Chemistry, La Serena, January 1982; M. Scholz and J.A. Valderrama, Bol. Soc. Chil. Quím., 27, 129 (1982); Chem. Abstr., 97, 23399d (1982).
9. M.J. Huges and A.J. Waring, J. Chem. Soc. Perkin Trans.II, 1043 (1974) and references cited therein.
10. This substance was prepared in 78% yield from cyclopentanecarboxaldehyde and morpholine in benzene solution, using the azeotropic procedure [G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz and R. Terrell, J. Am. Chem. Soc., 85, 207 (1963)]; b.p. 126-128°C/18 mm; IR (neat): 1630 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.63 (m, 4H), 2.30 (m, 4H), 2.81 (t, 4H, J≈5Hz), 3.71 (t, 4H, J≈5Hz), 5.54 (br s, 1H) ppm.
11. R. Cassis and J. Valderrama, Synth. Commun., 13, 347 (1983).
12. V. Balogh, M. Fetizon and M. Golfier, J. Org. Chem., 36, 1339 (1971).
13. Y. Miyagi, K. Kitamura, K. Maruyama and Y.L. Chow, Chem. Lett., 33 (1978).
14. E. Korusawa, Bull Chem. Soc. Jpn., 34, 300 (1961).
15. All new compounds gave satisfactory elemental analyses and spectroscopic data.

(Received in USA 9 August 1985)