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REACTION OF DILITHIATED 1,2-DIESTERS WITH β-BROMOETHYLOXIRANE.
SYNTHESIS OF ANNELATED γ-LACTONES

Peter J. Garratt and John R. Porter

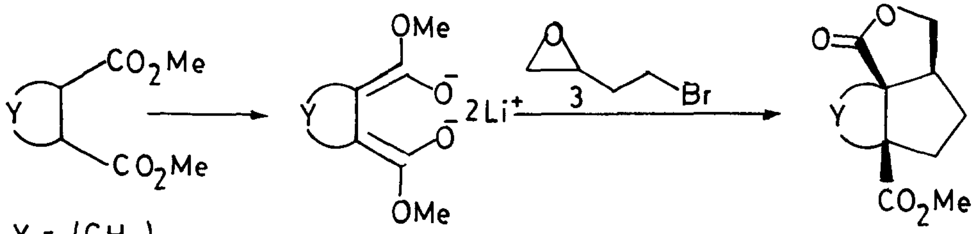
Department of Chemistry, University College London

20 Gordon Street, London WC1H 0AJ.

Summary: The reaction of cyclic vicinal diester dianions with β-bromoethyloxirane gives annelated γ-lactones.

Some time ago we described the reaction of dilithiated 1,2-diesters with α,ω-dihalides and ω-haloesters,[1] and these reactions have been exploited by ourselves[2] and others.[3] We have examined a variety of other electrophiles with these dilithiated species and now report that their reaction with β-bromoethyloxirane (3) gives annelated γ-lactones as readily isolable products in modest yield.

The 1,2-diester 1a-c was treated with 2 equivalents of LDA in THF containing HMPA at low temperature as previously described.[1] The resulting solution of the dianion 2a-c was added (syringe or cannula) to a stirred solution of 3 in THF at 0-5 °C over 30 min - 1 h. The solution was allowed to warm to rt, stirred for 14 h, when work-up and flash chromatography gave 4a - c as crystalline compounds.

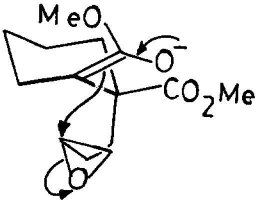


1a Y = $(CH_2)_3$
b Y = $(CH_2)_4$
c Y = $CH_2CH{=}CHCH_2$

2a-c

4a-c

The structures assigned to 4a - c are based on the spectral properties.[4,5] We have previously shown with other electrophiles that annelation occurs in a syn fashion[1] and the cis orientation of the ester and lactone groups is based on this and the unlikelihood that 4a would have the two 5-membered rings trans-fused. We assume that the reaction proceeds by initial displacement of the bromide followed by intramolecular ring opening of the epoxide 5. The epoxide would 'normally'[6] be expected to be attacked at the unsubstituted position under basic conditions and Baldwin's Rules[7] allow both processes (5-*Exo-Tet* and 6-*Exo-Tet*) but only one lactone is observed.[8] Assuming that the carbon of the enolate is sp^2, then models suggest that it is sterically more difficult for the unsubstituted carbon to approach within bonding distance of the enolate carbon in the required configuration than it is for the substituted carbon. This, together with the entropic preference, seems to lead to 5-membered rather than 6-membered ring formation. Our failure to obtain lactones from γ-bromopropyloxirane and the dianions 2a-c supports this view, but the low yields preclude a secure analysis of the process. The reaction forms two rings with the relative stereochemistry of three centres fixed and may be applicable to more complex systems. We are currently investigating the scope of this reaction.



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References and Notes

1. See Bilyard, K.G.; Garratt, P.J.; Hunter, R.; Lete, E. *J. Org. Chem.* 1982, *47*, 4731 and refs therein.

2. See Doecke, C.W.; Garratt, P.J.; Shariari-Zavareh, H.; Zahler, R. *J. Org. Chem.* 1984, *49*, 1412.

3. Long, N.R.; Rathke, M.W. *Synthetic Commun.* 1981, *11*, 687; Datta, S.C.; Franke, R.W.; Noire, P.D. *J. Org. Chem.* 1984, *49*, 2785; Girard, C.; Bloch, R. *Tetrahedron Lett.* 1982, *23*, 3683; Furata, K.; Misumi, A.; Mori, A.; Ikeda, N.; Yamamoto, H. *ibid*, 1984, *25*, 669; Misumi, A.; Furata, K.; Yamamoto, H. *ibid*, 1984, *25*, 671; Mundy, B.P.; Wilkening, D.; Lipkowitz, K.B. *J. Org. Chem.* 1985, *50*, 5727.

4. 4a: 22%, mp 59-61 °C, MS, *m/e* 224.1036 ($C_{12}H_{16}O_4$ requires 224.1048), 224, 192, 191, 183, 164, 151, 121; ^1H NMR, δ 4.37 (ABX,1H,J = 9.4, 8.2 Hz), 4.08 (ABX,1H,J = 9.4, 4.9 Hz), 3.66 (s,3H), 2.78 - 1.54 (m, 11H); ^{13}C NMR, δ 188.9, 175.1, 69.9, 65.8, 52.3, 49.1, 38.7, 38.2, 36.3, 31.7, 26.1; IR, 1762, 1720 cm^{-1}.

   4b: 37%, mp 86-88 °C; MS, *m/e* 238.1185 ($C_{13}H_{18}O_4$ requires 238.1204), 238, 206, 184, 178, 135, 121, 119; ^1H NMR, δ 4.36 (ABX,1H,J = 9.3, 6.3 Hz), 4.14 (ABX,1H,J = 9.3, 1.2 Hz), 3.76 (s,3H), 2.76 (m,1H), 2.31-1.20 (m,12H); ^{13}C NMR, δ 180.0, 174.4, 73.1, 56.7, 52.75, 51.6, 41.9, 34.75, 30.7, 28.8, 20.9, 20.8; IR, 1762, 1728 cm^{-1}.

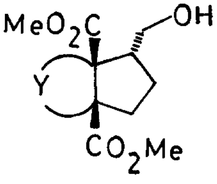
   4c: 30%, mp 94-96 °C; MS, *m/e* 236.1032 ($C_{13}H_{16}O_4$ requires 236.1048), 236, 204, 176, 148, 131, 117, 91, 69; ^1H NMR, δ 5.80 (br d,2H,J = 2.7 Hz), 4.36 (ABX,1H,J = 9.5, 5.7 Hz), 4.20 (ABX,1H,J = 9.3), 3.74 (s,3H), 2.64-1.99 (m,7H), 1.79-1.66 (m,2H); ^{13}C NMR, δ 180.0, 174.6, 125.3, 72.9, 55.8, 51.9, 51.6, 44.3, 35.1, 31.4, 28.7, 28.0; IR, 1762, 1728 cm^{-1}.

5. Satisfactory microanalyses have been obtained for all new compounds.

6. Parker, R.E.; Isaacs, N.S. *Chem. Rev.* 1959, *59*, 737.

7. Baldwin, J.E. *J. Chem. Soc. Chem. Comm.* 1976, 734.

8. The other major product isolated in each reaction is the corresponding alcohol to which we have assigned cis-trans stereochemistry with respect to the two ester groups and the alcohol carbon.



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