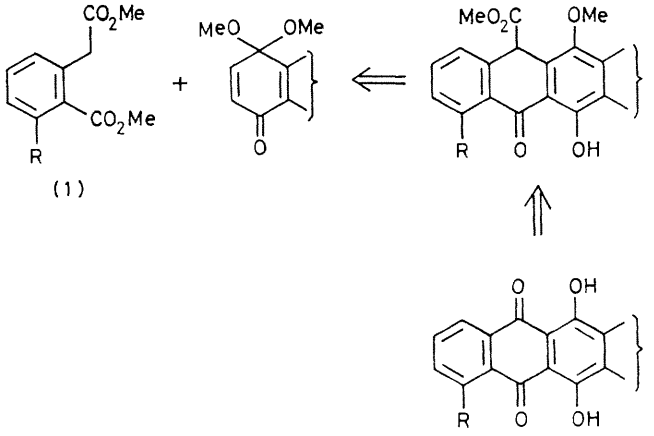
Regiospecific One-step Annelations *via* Quinone Monoacetals

By BERTRAND L CHENARD, D KEITH ANDERSON, and JOHN S SWENTON*
(*Department of Chemistry, The Ohio State University, Columbus, Ohio* 43210)

Summary Quinone monoacetals react with dimethyl homophthalate (methyl 2-methoxycarbonylphenylacetate) in the presence of base to afford anthrone derivatives under mild conditions

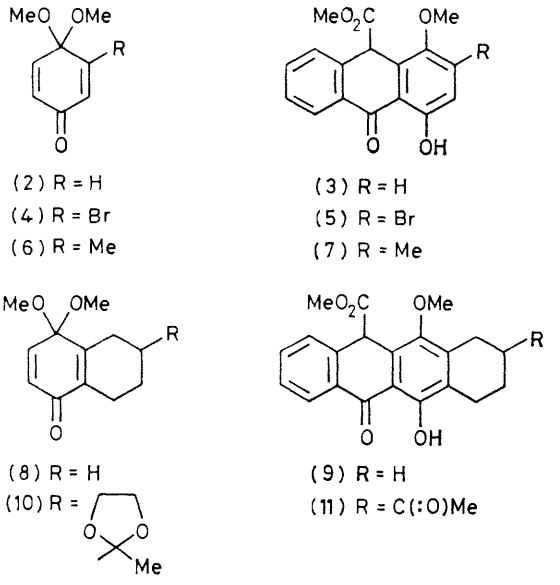
NEW routes to anthraquinone derivatives have been of much recent interest owing to their utility in anthracyclinone synthesis[1] Since highly functionalized quinone monoacetals are readily available *via* hydrolysis of one acetal group of electrochemically derived quinone bisacetals,[2] the annelation reactions of these compounds have potential value in anthracyclinone syntheses (Scheme)



SCHEME Strategy for anthracyclinone synthesis *via* annelation of quinone monoacetals, arrows are used 'retrosynthetically

Schmid[3,4] had previously shown that esters of homophthalic acid (2-carboxyphenylacetic acid esters) underwent annelation reactions with α,β-unsaturated ketones and esters Furthermore, Parker[5] has recently reported Michael additions of soft carbon nucleophiles to quinone monoacetals We present here a one-step regiospecific annelation reaction of dimethyl homophthalate to quinone monoacetals to produce tri- and tetra-cyclic anthrone ring systems

When dimethyl homophthalate (**1**, R = H) (1 mmol) was added to a tetrahydrofuran solution of (**2**) (1 mmol) containing 2 1 mmol of sodium hydride, the solution gradually turned deep red It was stirred at 25 °C for 1 day, and acidification and filtration through a short silica gel column (20% ether–light petroleum as eluant) then gave (**3**) in 60% recrystallized yield The structure of (**3**) was supported by its i r, high-resolution mass, ^{13}C n m r and most convincingly by its ^{1}H n m r spectra ($CDCl_3$, 60 MHz) δ 12 2 (s, 1H), 8 4—8 2 (m, 1H), 7 85—7 35 (m, 3H), 7 05 (ABq, Δν 14 Hz, *J* 9 Hz, 2H), 5 23 (s, 1H), 3 83 (s, 3H), and 3·6 (s, 3H)



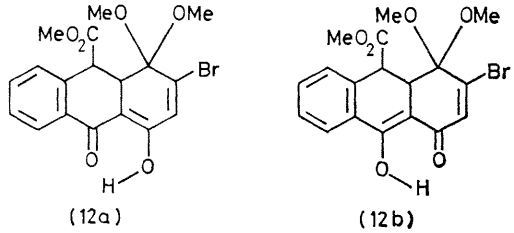
The reaction of (**1**) with (**4**), (**6**), (**8**), and (**10**) (Table) did not proceed directly to the aromatic compound, but instead afforded an acetal In the case of (**4**), this intermediate (**12**) was isolated and characterized m p 115—116 °C, ^{1}H n m r

TABLE Reaction of dimethyl homophthalate (**1**, R = H) with quinone monoacetals

Quinone monoacetal	Product	% Yield[a]	M p /°C
(**2**)	(**3**)	60	140—141[b]
(**4**)	(**5**)[c]	20	154 5—155 5[b]
(**6**)	(**7**)[c]	40	129—130[b]
(**8**)	(**9**)[c]	60	160—161[d]
(**10**)[e]	(**11**)[f]	41	193—197[d]

[a] Yield of recrystallized product not optimized [b] From ether–hexane [c] After heating with toluene *p* sulphonic acid hydrate in benzene [d] From methanol–CH_2Cl_2 [e] Prepared from the bromobisacetal (ref 2c) by hydrolysis of one acetal group reduction ($NaBH_4$) debromination (BuLi) and electrochemical oxidation [f] After treatment with aqueous THF and HCl obtained as a mixture of diastereoisomers

($CDCl_3$, 90 MHz) δ 15 6 (s 1H), 8 0—7 85 (m, 1H), 7 5—7 25 (m 2H) 7 15—7 0 (m, 1H), 6 85 (s 1H), 4 22 (ABq, Δν 48 Hz *J* 14 Hz 2H) 3 85 (s, 3H) 3 5 (s, 3H) and 3 4 (s 3H) While the data do not rigorously distinguish between tautomers (**12a**) and (**12b**), the enolic proton at δ 15 6



excludes the diketone tautomer. In the other systems, this acetal intermediate was not isolated; rather the crude product was heated with toluene-*p*-sulphonic acid hydrate in benzene or stirred at room temperature with aqueous acid to effect elimination of methanol to give (**7**), (**9**), or (**11**).

While the yield of these annelations is modest, the ease of product isolation (direct crystallization or filtration of the crude reaction mixture through silica gel) makes this a convenient route to the anthrone systems. Furthermore, the availability of a variety of homophthalates[6] and quinone monoacetals makes this reaction sequence an especially versatile route to linear tri- and tetra-cyclic ring systems. Other annelation reactions[5] of quinone monoacetals will be reported in our full manuscript.

We thank the National Institutes of Health and the National Science Foundation for support of this work.

(*Received*, 30*th June* 1980; *Com.* 713.)

[1] For an excellent review, see F. Arcamone, 'Topics in Antibiotic Chemistry,' ed. P. G. Sammes, Halsted Press, New York, 1978, Vol. **2**, Ch. **3**.

[2] M. J. Manning, D. R. Henton, and J. S. Swenton, *Tetrahedron Lett.*, 1977, **333**; D. R. Henton, B. L. Chenard, and J. S. Swenton, *J. Chem. Soc., Chem. Commun.*, 1979, **326**; D. R. Henton, D. K. Anderson, M. J. Manning, and J. S. Swenton, *J. Org. Chem.*, 1980, **45**, **3422**, and references cited therein.

[3] W. Eisenmuth, H. B. Renfroe, and H. Schmid, *Helv. Chim. Acta*, 1965, **48**, 375.

[4] For leading references to related transformations, see: F. M. Hauser and S. Prasanna, *J. Org. Chem.*, 1979, **44**, 2596; N. J. P. Broom and P. G. Sammes, *J. Chem. Soc., Chem. Commun.*, 1978, 162; G. A. Kraus and H. Sugimoto, *Tetrahedron Lett.*, 1978, 2263.

[5] K. A. Parker and S. Kang, *J. Org. Chem.*, 1980, **45**, 1218.

[6] A. P. Kozikowski and R. Schmiesing, *Syn. Commun.*, 1978, **8**, **363**.