Regiospecific Alkylation of Phenols: *ortho* or *para* to *α* Coupling in Cyclization of Bis-phenols *via* Quinone Methides

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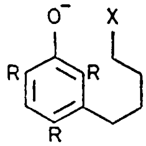
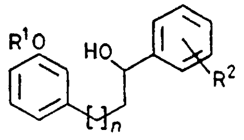
Summary Intramolecular alkylations of phenols by *o*- and *p*-hydroxybenzylic alcohols are achieved with high regioselectivity by heating the bis-magnesium salts of bis-phenols such as (**2**) and (**5**), which cyclise efficiently into aryl-indanols and aryltetralols.

FOLLOWING our successful Ar$_2^-$-6 cyclisation of phenoxide anions of general type (**1**) using achiral[1] and chiral[2] leaving groups, we attempted the analogous cyclisation involving an enone electron sink. Quinone methides were considered likely candidates since (a) the precursors are readily prepared, (b) aromatization provides a strong driving force, and (c) studies[3] on intermolecular systems indicated that intramolecular magnesium(II) chelation could induce regiospecificity.

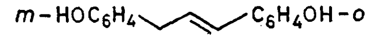


(**1**)
a; R = H
b; R = Me

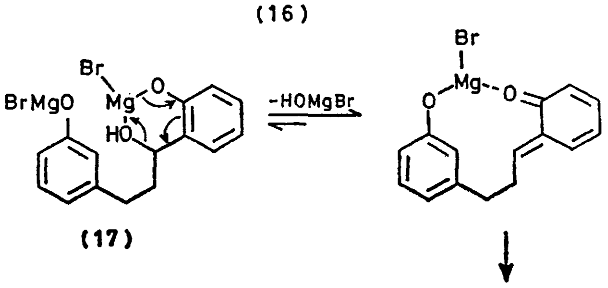


(**2**) n = 1, R¹ = H, R² = *o*-OH
(**3**) n = 1, R¹ = H, R² = *o*-OMe
(**4**) n = 1, R¹ = Me, R² = *o*-OH
(**5**) n = 2, R¹ = H, R² = *o*-OH
(**6**) n = 1, R¹ = H, R² = *p*-OH
(**7**) n = 2, R¹ = H, R² = *p*-OH

The carbinol (**2**)† (1 mol) was heated under reflux for 20 h in benzene with ethylmagnesium bromide[3,4] (2 mol). The bis-phenol (**8**)† was formed (71%)‡ together with the dehydration product (**16**) (11%).‡ G.l.c.§ of the dimethyl ether of (**8**) indicated that only a trace (< 1%) of (**12**) had been formed. In contrast, when the carbinol (**2**) was cyclised (SnCl$_4$, CH$_2$Cl$_2$), a mixture (72%)‡ of (**8**) and (**12**) in the ratio 5:95 respectively was formed. The striking regiospecificity of the Mg$^{\text{II}}$-induced cyclisation is accounted for in the mechanism in the Scheme. The evidence for this is based on the following results: (a) (**2**) did not cyclise when heated with either NaH or BuLi in benzene, (b) the bis-magnesium salt (**17**) (1 mol) did not cyclise under standard conditions when 18-crown-6 (2 mol) was present, (c) (**16**) (1 mol) was recovered unchanged when heated with ethylmagnesium bromide (2 mol) in benzene, (d) under standard conditions neither (**3**),† (**4**),† nor (**18**)† cyclised, and (e) the *o*-quinone methide formed from the phenol (**19**) was trapped with ethyl vinyl ether[5] to yield the cycloadduct (**20**) (55%).‡ High *ortho*-regiospecificity is again evident in the cyclisation of the homologue (**5**).† A mixture of (**9**)† and (**13**)† in the ratio 88:12§ was isolated (90%).‡ The increased percentage of *para*-alkylation indicates a more weakly complexed quinone methide intermediate than that derived from (**17**) (Scheme). The ease of six-membered ring formation is highlighted by the high yield (90%)‡ of cyclised product obtained from (**5**) (1 mol) even in the presence of 18-crown-6 (2 mol). In this instance the ratio of (**9**) to (**13**) was 38:62.§



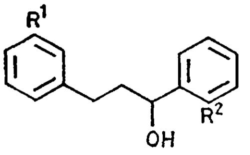
(**16**)



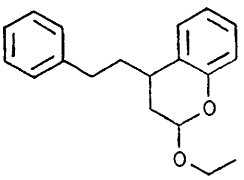
SCHEME

The triols (**6**)† and (**7**)† were investigated to probe the characteristics of *p*-quinone methide cyclisations. Since intramolecular Mg$^{\text{II}}$ bridging would not then be involved, we expected (a) inefficient cyclisation of (**6**), (b) efficient cyclisation of (**7**), and (c) higher *para*- to *ortho*-regiospecificity. In the event, (**6**) cyclised (43%)‡ to (**10**)† and (**14**)† in the ratio 10:90§ and (**7**) cyclised (90%) to (**11**)† and

(**8**)	n = 1, R = *o*-OH	(**12**)
(**9**)	n = 2, R = *o*-PH	(**13**)
(**10**)	n = 1, R = *p*-OH	(**14**)
(**11**)	n = 2, R = *p*-OH	(**15**)



(**18**) R¹ = OH, R² = H
(**19**) R¹ = H, R² = OH



(**20**)

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† The ^{1}H n.m.r. and analytical data are in accord with this structure.

‡ Isolated yield.

§ Determined by g.l.c. of the dimethyl ethers using a 2 m column of 2½% CEMS on Chromosorb G with a programmed temperature increase in the range 150—200 °C.

(**15**)† in the ratio 7:93.§ By comparison, cyclisation ($SnCl_4$, CH_2Cl_2) of the dimethyl ether of (**7**)† gave a product mixture (71%)‡ with an *ortho* to *para* ratio of 10:90.§ The high *para*-regiospecificity of *p*-quinone methides is most probably due to steric hindrance of the *ortho*-position by the magnesium cation in the bis-Mg^{II} phenoxide salts of both (**6**) and (**7**). Thus, for example, cyclisation of the bis-Mg^{II} salt of (**7**) (1 mol) in the presence of 18-crown-6 (2 mol) occurred (83%)‡ with the formation of (**11**) and (**15**) in the ratio of 40:60§ respectively.

(*Received*, 30*th January* 1979; *Com.* 088.)

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