

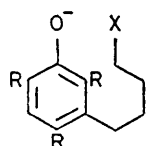
Regiospecific Alkylation of Phenols: *ortho* or *para* to α Coupling in Cyclization of Bis-phenols *via* Quinone Methides

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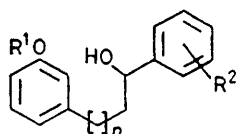
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Summary Intramolecular alkylations of phenols by *o*- and *p*-hydroxybenzylic alcohols are achieved with high regioselectivity by heating the bis-magnesium salts of bis-phenols such as (2) and (5), which cyclise efficiently into aryl-indanols and aryltetralols.

FOLLOWING our successful Ar_2^-6 cyclisation of phenoxide anions of general type (1) using achiral¹ and chiral² 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) studies³ on intermolecular systems indicated that intramolecular magnesium(II) chelation could induce regioselectivity.



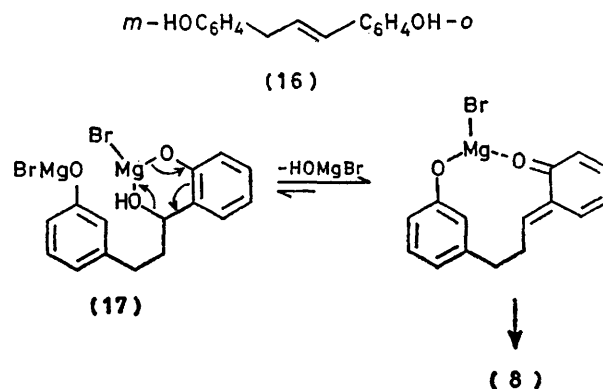
(1)
a; R = H
b; R = Me



(2) $n = 1$, $R^1 = \text{H}$, $R^2 = o\text{-OH}$
(3) $n = 1$, $R^1 = \text{H}$, $R^2 = o\text{-OMe}$
(4) $n = 1$, $R^1 = \text{Me}$, $R^2 = o\text{-OH}$
(5) $n = 2$, $R^1 = \text{H}$, $R^2 = o\text{-OH}$
(6) $n = 1$, $R^1 = \text{H}$, $R^2 = p\text{-OH}$
(7) $n = 2$, $R^1 = \text{H}$, $R^2 = p\text{-OH}$

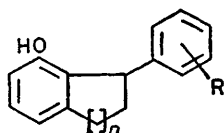
The carbinol (2)[†] (1 mol) was heated under reflux for 20 h in benzene with ethylmagnesium bromide^{3,4} (2 mol). The bis-phenol (8)[†] was formed (71%)[‡] together with the dehydration product (16) (11%).[‡] G.l.c.§ of the dimethyl ether of (8) indicated that only a trace (< 1%) of (12) had been formed. In contrast, when the carbinol (2) was cyclised (SnCl_4 , CH_2Cl_2), a mixture (72%)[‡] of (8) and (12) in the ratio 5:95 respectively was formed. The striking regioselectivity of the Mg^{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 ether⁵ to yield the cyclo-adduct (20) (55%).[‡] High *ortho*-regioselectivity 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.§

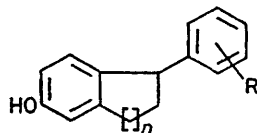


SCHEME

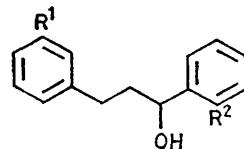
The triols (6)[†] and (7)[†] were investigated to probe the characteristics of *p*-quinone methide cyclisations. Since intramolecular Mg^{II} bridging would not then be involved, we expected (a) inefficient cyclisation of (6), (b) efficient cyclisation of (7), and (c) higher *para*- to *ortho*-regioselectivity.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



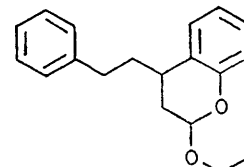
(8) $n = 1$, R = *o*-OH
(9) $n = 2$, R = *o*-PH
(10) $n = 1$, R = *p*-OH
(11) $n = 2$, R = *p*-OH



(12)
(13)
(14)
(15)



(18) $R^1 = \text{OH}$, $R^2 = \text{H}$
(19) $R^1 = \text{H}$, $R^2 = \text{OH}$



(20)

[†] The ^1H 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 2% CEMS on Chromosorb G with a programmed temperature increase in the range 150–200 °C.

(15)[†] in the ratio 7:93.§ By comparison, cyclisation (SnCl₄, CH₂Cl₂) 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.

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³ G. Casiraghi, G. Casnati, M. Cornia, A. Pochini, G. Sartori, and R. Ungaro, *J.C.S. Perkin I*, 1978, 322.

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