Tetrahedron Letters No. 43, pp 3745 - 3748, 1975. Pergamon Press. Printed in Great Britain.

HYDROGEN TRANSFER BY KETYL RADICALS: THE REDUCTIVE DIMERIZATION OF QUINONE METHIDES

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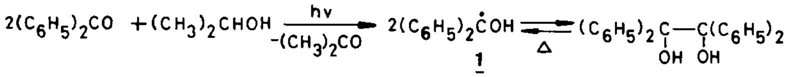
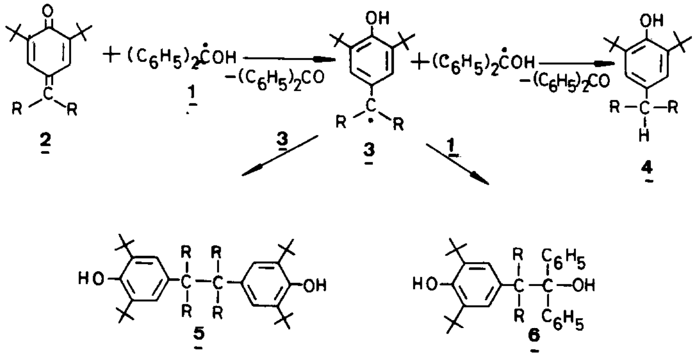
(Received in UK 18 August 1975; accepted for publication 15 September 1975)

Diphenylhydroxymethyl radical (1), either formed photochemically by irradiation of benzophenone in isopropanol, or generated thermally by dissociation of benzpinacol in solution, is readily oxidized by hydrogen acceptors A to give benzophenone and the hydrogenated acceptor, AH_2.[1-4] For example, the α,α-diphenyl-substituted quinone methide 2a can thus be reduced to the triphenylmethane 4a.[3]



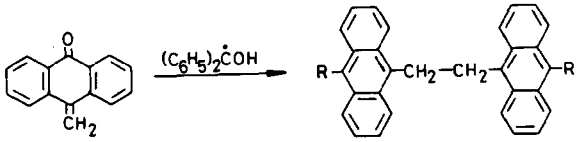
$$2(C_6H_5)_2CO + (CH_3)_2CHOH \xrightarrow[-(CH_3)_2CO]{h\nu} 2\underset{1}{(C_6H_5)_2\dot{C}OH} \underset{\Delta}{\rightleftharpoons} (C_6H_5)_2\underset{OH}{C}-\underset{OH}{C}(C_6H_5)_2$$



2-5	R
a	C_6H_5
b	CH_3
c	H

Unexpectedly, we have now found that the reduction of quinone methides by ketyl radical 1 will take a different course when the phenyl groups in 2a are replaced by sterically less bulky groups such as methyl or hydrogen. Thus, refluxing a solution of α,α-dimethyl-2,6-di-t-butylquinone methide (2b, 3 mmol) and benzpinacol (1.5 mmol) in xylene (20 ml) for 15 min under nitrogen does not give any phenol 4b but gives dimer 5b[5] in 82% yield. Likewise, the reaction of the elusive[6] quinone methide 2c (2.5 mmol) and benzpinacol (2.5 mmol) in boiling xylene (20 ml) for 15 min yields the substituted bibenzyl 5c (80%) together with a small amount (9%) of the mixed coupling product 6 (mp 160-162°). The formation of 6 suggests that hydrogen atom transfer from ketyl radical 1 to quinone methides leads to 4-hydroxybenzyl radicals 3 which, under the experimental conditions[7], preferentially dimerize to give bibenzyls 5 rather than undergoing further reduction to 4.

Since the hydrogen transfer by ketyl radicals proceeds in neutral solution, this method obviously can be of preparative advantage by comparison with other means of reduction. For example, 10-methyleneanthrone (7) is known to be reduced by zinc in the presence of ammonia to give 1,2-di-9-anthrylethane (8a).[8,9] By contrast, refluxing a solution of methyleneanthrone (20.6 g; 0.1 mol) and benzpinacol (18.3 g; 0.05 mol) in xylene (300 ml) under nitrogen for 25 min yields the heretofore not accessible primary dimerization product 1,2-bis(10-hydroxy-9-anthryl)ethane (8b) which precipitates from the reaction mixture and can be isolated in 75% yield; (greenish-yellow fluorescent needles, mp > 150°). Although dimer 8b was found to be highly reactive in solution, its structure is supported by elemental analysis, spectral data (IR, MS) and by the formation of the stable derivatives 8c (mp 295°) and 8d (mp 190°).[10]



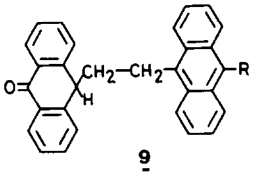
7

8

8	R
a	H
b	OH
c	OAc
d	$OSiMe_3$

In DMSO or DMF solution, 8b readily tautomerized to give the unstable new isomer 9a (mp 285°; 80% yield) which precipitated and was characterized by its stable trimethylsilyl[11] derivative 9b (mp 169-172°). Isomerization of 9a in ethanol solution, catalyzed by $NaOCH_3$, gave the previously unknown tautomeric dimer 10a (mp 245°; 92% yield) which upon reduction with zinc in aqueous ammonia ideed gave the known[9,12] di-anthrylethane 8a (63% yield) (see Fig 1).

Upon exposure to air, solutions of dimer 8b in methylene chloride or methyl acrylate rapidly decolorize and deposit the crystalline bis-hydroperoxy compound 10b (mp 295°; 90% yield) which formed a bis-tri-methylsilyl ether 10c (mp 245°) by treatment with BSA in dioxane. Catalytic hydrogenation of 10b proceeded smoothly to give the dihydroxy compound[13] 10d (mp 350°; 73% yield), whose diethyl ether 10e was obtained by oxidation of dimer 10a with DDQ in ethanol-containing chloroform. By contrast, dehydrogenation of dimer 8b by DDQ in boiling dioxane resulted in the known[14] 1,2-bis(9'-oxo-10'-anthrylidene) ethane 11 (65% yield). Upon reduction by thermally generated ketyl radicals 1 in boiling xylene under nitrogen, "stilbenequinone" 11 gave the new 1,2-bis(10'-hydroxy-9'-anthryl)ethylene 12a[15] in 96% yield. It readily reverted to 11 upon exposure to air, however, the bis-trimethylsilyl ether 12b (mp 185°) was found to be stable towards autoxidation thus allowing UV-spectroscopic measurements to be made for comparison purposes (see Fig 1).



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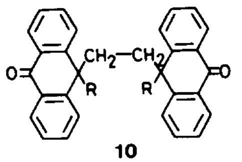
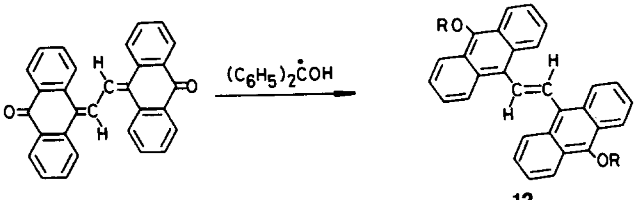


10

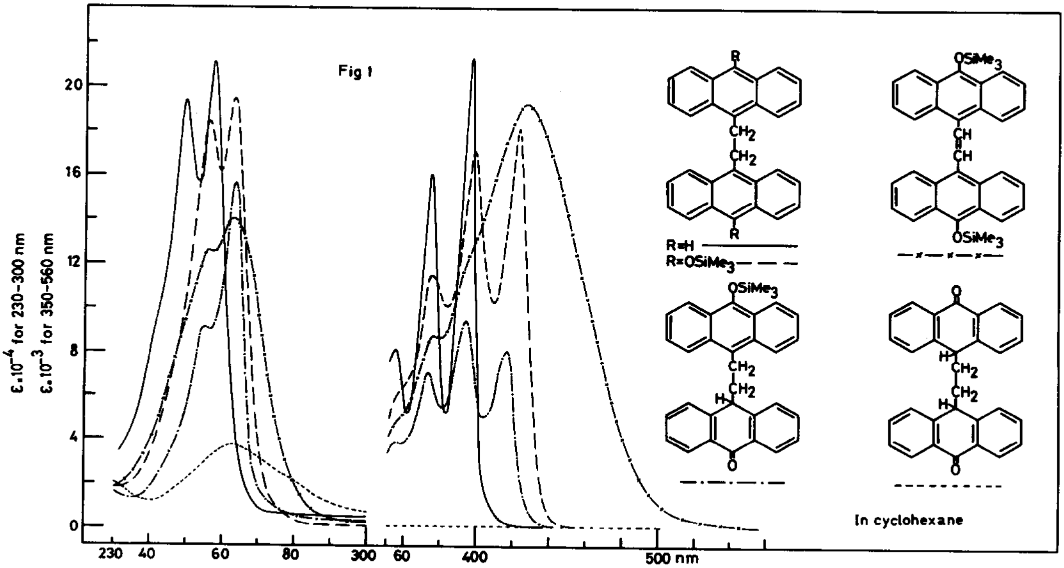
9	R
a	OH
b	$OSiMe_3$

10	R
a	H
b	OOH
c	$OOSiMe_3$
d	OH
e	OC_2H_5



11 12

12	R
a	H
b	$SiMe_3$



The reaction of ketyl radical **1** with quinone methides not only is of synthetic interest but also sheds light on the controversial "rearrangement" of 4-methylphenoxy radicals into 4-hydroxybenzyl radicals.[16] Recent kinetic data indicate the involvement of quinone methides in this transformation.[17] Our results show that hydrogen transfer from suitable hydrogen donors to quinone methides indeed can be an efficient process for the generation of 4-hydroxybenzyl radicals.

References and Footnotes

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