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SYNTHESIS OF NON-K-REGION ORTHO-QUINONES OF POLYCYCLIC AROMATIC HYDROCARBONS FROM CYCLIC KETONES

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Summary: Non-K-region o-quinones of polycyclic aromatic hydrocarbons are prepared in four steps from cyclic ketones via dehydrogenation of tetrahydrodiols with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

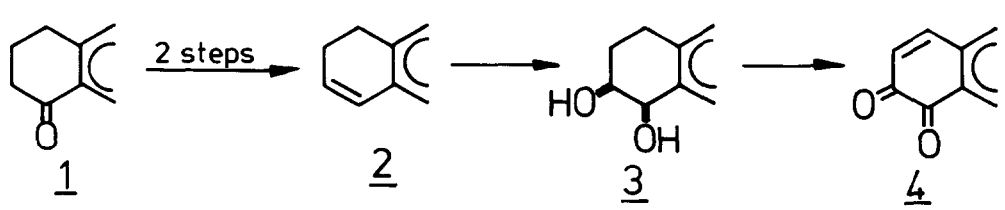
Several quinones are metabolic products of the carcinogenic polycyclic aromatic hydrocarbon benzo[a]pyrene.[1,2] Non-K-region o-quinones have not yet been identified as metabolites of polycyclic aromatic hydrocarbons although it is likely that they are formed by autoxidation of phenols or of catechols which can be produced from dihydrodiols by dihydrodiol dehydrogenase,[3,4] an enzyme which has therefore been inferred as an important control in chemical mutagenesis and carcinogenesis.[5]

In order to elucidate the role of non-K-region o-quinones in the metabolism and toxicological activities of polycyclic aromatic hydrocarbons the synthetic reference compounds are urgently needed.

The syntheses of the non-K-region o-quinones of naphthalene,[6] anthracene[7] and phenanthrene (4a,[8] 4b[9]) were described more than fifty years ago. More recently the preparation of 4e,[10] 4f,[11,12] 4i,[13] benz[a]anthracene-3,4-dione,[12] 7-methylbenz[a]anthracene-3,4-dione[14] and of 7,12-dimethylbenz[a]anthracene-3,4-dione[12,15] have been reported. A generally applicable method for the synthesis of the non-K-region o-quinones of other polycyclic aromatic hydrocarbons is, however, still lacking.

We now wish to report the facile preparation of non-K-region o-quinones of polycyclic aromatic hydrocarbons, 4, by heating a solution of a tetrahydrodiol, 3, with 12 equiv. 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)

SCHEME



1 2 3 4

in dioxane (reflux, 24 h). DDQ not only oxidizes the 1,2-diol to the α-diketone but also introduces the olefinic double bound of the o-quinone.

When we first discovered this one-step conversion in the case of 4f we attributed the surprisingly facile generation of the o-quinone to the ease of double bond formation at the bay-region[16] as described for several polycyclic aromatic hydrocarbons.[17] Yet our results indicate (TABLE) that the reaction is not restricted to the synthesis of non-bay-region o-quinones (e.g., 4a, 4d, 4f, 4i) but is also applicable to the preparation of bay-region o-quinones (e.g., 4b, 4c, 4e, 4g, 4h). Thus our method is both simpler and more general than the recently published synthesis of non-K-region o-quinones.[12]

The complete pathway which we developed to synthesize several hitherto unknown non-K-region o-quinones is depicted in the SCHEME. The cyclic ketones 1, some of which are commercially available, can be prepared either by the classic HAWORTH method[18] or by direct introduction of the carbonyl function into tetrahydro arenes.[19] 1 is then reduced to the alcohol and dehydrated to the alkene 2 as has been described for many aromatic hydrocarbons.[20,21] 2 is cis-dihydroxylated with a catalytic amount of osmium(VIII)-oxide in the presence of N-methylmorpholine N-oxide[22,23] to yield 3.

Our synthetic approach constitutes a new method for the preparation of non-K-region o-quinones and seems to be generally applicable. Research on this aspect is in progress in our laboratory.

Simultaneously we are investigating the biological potential of the newly synthesized o-quinones.

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29. Spectral data of the new compounds:

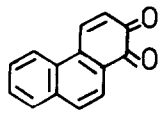
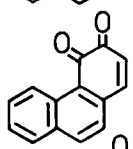
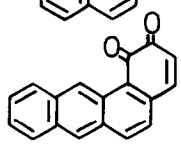
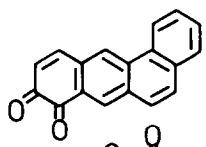
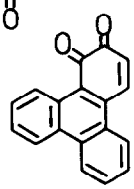
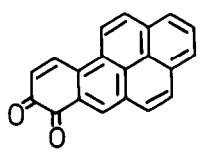
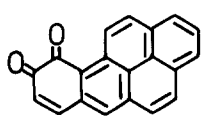
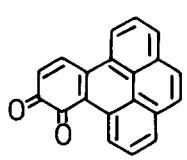
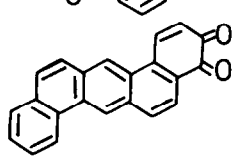
4c, ^{1}H NMR (60 MHz, CD_2Cl_2) δ [ppm] 6.47 (d, 1, H_3, $J_{3,4}$ = 9.9 Hz), 7.31 - 8.51 (m, 8, aromatic), 10.02 (br. s, 1, H_{12}); VIS-UV (dioxane) λ_{max} [nm] (log ε) 313 (4.11), 344 (3.75), 424 (3.63), 510 (2.76); IR (KBr) $\nu_{C=O}$ [cm^{-1}] 1652; MS (70 eV) m/e (rel. int.) 258 (15.5%, M^+), 230 (100%, M - CO), 202 (39.9%, M - 2 CO).

4d, ^{1}H NMR (60 MHz, $CDCl_3$) δ [ppm] 6.47 (d, 1, H_{10}, $J_{10,11}$ = 10.8 Hz), 7.50 - 7.93 (m, 6, aromatic), 8.42 - 8.67 (m, 1, H_1), 8.48 (s, 1, H_{12}), 8.58 (s, 1, H_7); VIS-UV (dioxane) λ_{max} [nm] (log ε) 283 (4.41), 296 (4.39), 309 (4.42), 322 (4.42), 392 (3.55), 441 (3.62); IR (KBr) $\nu_{C=O}$ [cm^{-1}] 1652; MS (70 eV) m/e (rel. int.) 258 (13.9%, M^+), 230 (100%, M - CO), 202 (37.2%, M - 2 CO).

4g, ^{1}H NMR (90 MHz, CD_2Cl_2) δ [ppm] 6.52 (d, 1, H_8, $J_{7,8}$ = 9.9 Hz), 7.71 (d, 1, H_7), 8.02 - 8.47 (m, 7, aromatic), 9.66 (d, 1, H_{11}, $J_{11,12}$ = 9.9 Hz); VIS-UV (dioxane) λ_{max} [nm] (log ε) 277 (4.36), 310 (4.14), 334 (4.32), 350 (4.53), 400 (3.45), 484 (4.06); IR (KBr) $\nu_{C=O}$ [cm^{-1}] 1643; MS (70 eV) m/e (rel. int.) 282 (16.1%, M^+), 254 (100%, M - CO), 226 (32.2%, M - 2 CO).

4h, ^{1}H NMR (90 MHz, CD_2Cl_2) δ [ppm] 6.70 (d, 1, H_{11}, $J_{11,12}$ = 10.8 Hz), 8.09 - 8.78 (m, 8, aromatic), 9.68 (dd, 1, H_8, $J_{7,8}$ = 8.1 Hz, $J_{6,8}$ = 1.8 Hz); VIS-UV (dioxane) λ_{max} [nm] (log ε) 272 (4.46), 319 (4.23), 332 (4.26), 424 (3.61), 503 (3.39); IR (KBr) $\nu_{C=O}$ [cm^{-1}] 1649; MS (70 eV) m/e (rel. int.) 282 (22.6%, M^+), 254 (100%, M - CO), 226 (61.6%, M - 2 CO).

TABLE: SYNTHESIS OF NON-K-REGION ORTHO-QUINONES

Starting Material	o-Quinone[a] 4		Yield[b] %	m.p.[c] (Lit. m.p.) °C
1a[18]		4a	55	215 (216[8])
1b[18]		4b	63	133 (132-3[9])
1c[24]		4c[29]	41	173
1d[25]		4d[29]	51	238
1e[26]		4e	53	188 (188-190[10])
1f[27]		4f	65	264 (> 260[12])
2g[17]		4g[29]	62	237
1,2,3,6,7,8-hexahydro-1h[27]		4h[29]	30	212
1i[28]		4i	24	> 290 (301-2[13])

a Microanalyses were in good agreement with the calculated values (C ± 0.3; H ± 0.2). ^{1}H-NMR- and mass spectra were in accordance with the assigned structures.

b Yield (isolated product) refers to the last step (3→4).

c All melting points are uncorrected.

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