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THE CHEMISTRY OF PHENALENIUM SYSTEMS. XXIX[1)]

NOVEL RING CONTRACTION DURING m-CHLOROPERBENZOIC ACID OXIDATION OF MUTAGENIC AZULENO[1,2,3-cd]PHENALENE. A MODEL FOR METABOLIC ACTIVATION AND BINDING OF MUTAGENIC NONALTERNANT HYDROCARBON

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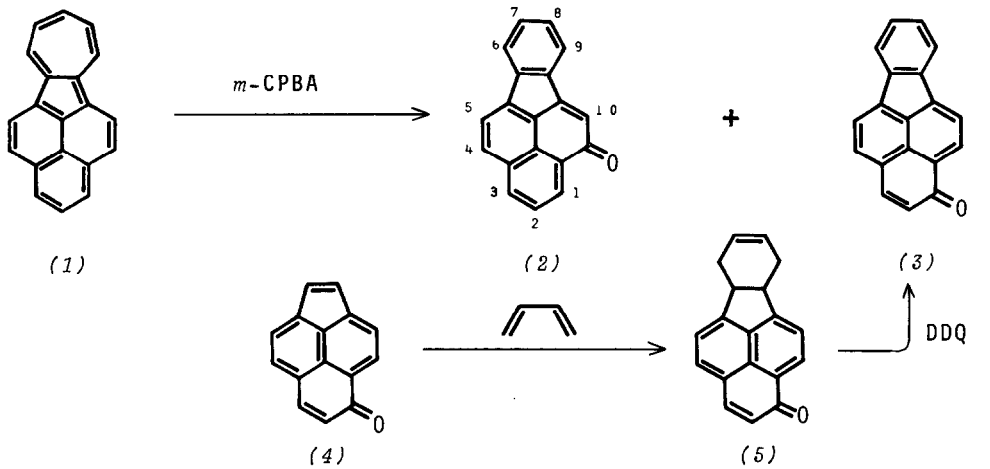
It has become apparent that mutagenic activity is known to be correlated to a great extent with carcinogenic activity in many synthetic and naturally occuring compounds.[2)] Since a novel nonalternant isomer of potent carcinogen benzo[*a*]pyrene, azuleno[1,2,3-*cd*]phenalene (*1*), synthesized by us,[3)] has been shown to be a highly mutagenic compound,[4)] the compound (*1*) was considered worthy of being submitted to examination of its chemical behaviours.

Because of their biological importance, considerable effort has recently been directed toward the synthesis and the binding reaction with cellular entities of arene oxides during the past several years.[5)] We have, therefore, investigated the action of *m*-chloroperbenzoic acid (*m*-CPBA) on *1*.

Reaction of *1* (0.1 mmol) with *m*-CPBA (0.2 mmol) in methylene chloride (4 ml) at room temperature for over night has now been found to give two crystalline isomeric products [$C_{19}H_{10}O$, M^+ m/e 254], separated by column chromatography on alumina along with 24 % recovery of *1*. Thus were obtained (*2*) [24%], dark red needles, mp 162-163°C from benzene-hexane, and (*3*) [16%], red needles, mp 179-184°C from benzene-hexane. The major product, *2*, [UV λ_{max} nm (log ε) in cyclohexane, 223(4.47), 254(4.47), 278(s, 4.61), 284(4.67), 304(3.99), 318(3.96),351 (3.74), 369(3.89), 389(3.76), 409(3.78), 458(3.29), 486(3.21), 523(2.83), 534 (2.71); IR (KBr) 1648(m), 1622 cm^{-1}(s); ^{1}H-NMR δ($CDCl_3$) 7.89(dd, J=8.1, 1.0 Hz,

H-3), 8.16(dd, J=7.2, 1.0 Hz, H-1), 6.69(s, H-10), 7.50(d, J=8.4 Hz H-5), 7.75 (d, J=8.4 Hz, H-4), 7.1-7.6(m, H-2, 6-9)[6]] was identified as 11-oxo-11*H*-benzo-[*cd*]fluoranthene based on comparison with the authentic sample,[7] while the minor product, *3*, was assigned as 1-oxo-1*H*-benzo[*cd*]fluoranthene from its spectral properties [UV λ_{max} nm (log ε) in cyclohexane, 243(4.56), 294(3.91), 307(3.94), 363(3.82), 379(4.03), 403(4.17), 426(4.21), 514(s, 2.67); IR (KBr) 1642(m), 1624 cm^{-1}(s); ^{1}H-NMR δ($CDCl_3$) three sets of AB-quartets at 6.43 and 7.44(J=9.8 Hz, H-2, 3), 7.57 and 7.44(J=7.2 Hz, H-4,5), and 7.75 and 8.28(J=7.5 Hz, H-10,11), and a four protons multiplet at 7.2-7.7[6]]. The final structural confirmation of *3* could be made unambiguously by the independent synthesis of *3* starting from the

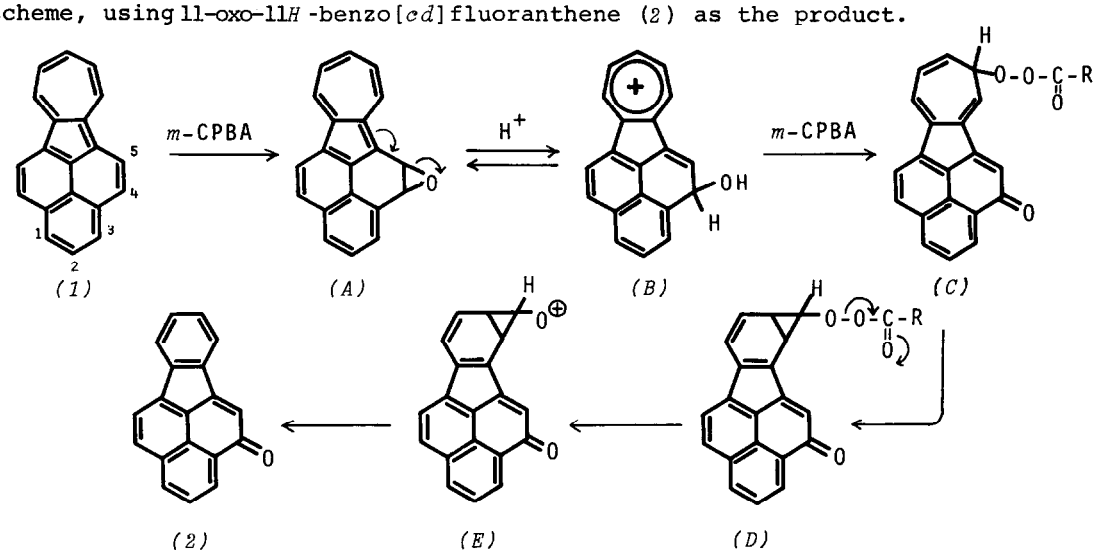


(1) *(2)* *(3)* *(4)* *(5)*

known tetracyclic ketone (*4*).[8] Thus, Diels-Alder reaction of *4* with butadiene (hydroquinone, 180°C, 12 h, in autoclave) produces the pentacyclic ketone (*5*) [yellow prisms, mp 162-163°C, ^{1}H-NMR δ($CDCl_3$) 6.67, 7.69(AB-q, J=9.8 Hz, H-2,3), 7.72, 7.34(AB-q, J=7.0 Hz, H-4,5), 7.55, 8.57(AB-q, J=8.0 Hz, H-10,11), 5.6-6.2 (m, H-7,8), 3.7-4.2(m, H-5b, 9a), 2.0-3.1(m, H-6,6',9,9')]. Dehydrogenation of *5* with dichlorodicyanobenzoquinone [refluxing benzene, 3 h] gives the fully conjugated ketone which was identical in all respects with *3*.

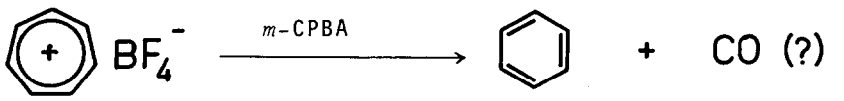
Because of the following—— (i) Oxidation of a double bond with peracid generally prodceeds by electrophilic attack of the reagent, (ii) azuleno[1,2,3-*cd*]phenalene (*1*) is known to form both 1- and 4-substituted products when subjected to Friedel-Crafts acylation and Vilsmeier formylation,[9] and (iii) the tropylium bromide readily form benzene and carbon monoxide when treated with

hydrogen peroxide[10] ——— we propose the mechanism shown in the following scheme, using 11-oxo-11*H*-benzo[*cd*]fluoranthene (*2*) as the product.



Initial electrophilic attack of *m*-CPBA to *1* would give an intermediate epoxide (A) that now is susceptible to nucleophilic attack at the seven-membered ring by a second molecule of *m*-CPBA because the stable tropylium ion structure (B) might reasonably be expected due to opening of the oxirane ring in an acidic medium. Nucleophilic attack of the oxygen atom of *m*-CPBA to the seven-membered ring carbon atom[11] accompanied with oxidation of the hydroxyl group affords the corresponding phenalenone (C). Valence bond isomerization of (C) into the norcaradiene intermediate (D), followed by loss of *m*-chlorobenzoate ion, would lead to the final intermediate (E), which can decompose with loss of carbon monoxide to the product (*2*). If the initial epoxidation was occured at 1,2-position of *1* instead of 4,5-position, then the oxidation of *1* should give the alternate product (*3*).

While many examples are available in the literature in which the tropylium ion was oxidized with various reagents to form benzenoid compounds,[10,12] oxidation of the tropylium ion with *m*-CPBA was not examined so far. In fact, like hydrogen peroxide oxidation, the tropylium tetrafluoroborate (1.5 mmol) was found to produce benzene in 60% yield when treated with *m*-CPBA (2 mmol) in methylene chloride at 0°C. This results provides the compelling evidence for the intermediacy of (B).



Since this ring contraction reaction consists of the activation of the seven-membered ring in *1* to the nucleophilic attack due to the formation of arene oxide followed by the binding with *m*-CPBA as an nucleophile, it is thought that this reaction will provide some model for the mutagenic and carcinogenic activity of *1*.[13] Current investigations are directed towards the synthesis of 1,2- and 4,5-epoxides of *1*.

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