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The Chemistry of Isopyrene (Azuleno[2,1,8-ija]azulene). Oxidations[#]

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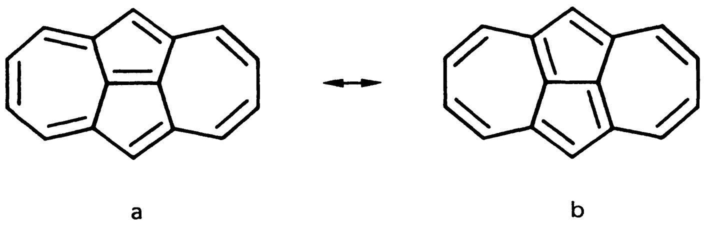
The nonbenzenoid aromatic hydrocarbon isopyrene undergoes some exceptional - synthetically useful - oxidative transformations. In accord with theoretical arguments, it reacts with bidentate oxidants preferentially at the "central C=C bond" to give bridged [14]annulenes with an anthracene perimeter.

Isopyrene (**1**) (azuleno[2,1,8-ija]azulene)[1)] is a planar resonance hybrid to which, on the basis of spectral[2)] and X-ray crystallographic[1b,3)] evidence, structure **1**a must make the major contribution. To a first approximation, **1** may therefore be regarded as a bridged [14]annulene with a central C=C cross-link as a perturbation. When seen from this point of view, **1** constitutes the parent of the bridged [14]annulenes with an anthracene perimeter that have emerged from the Cologne laboratory over the last two decades.[4)]



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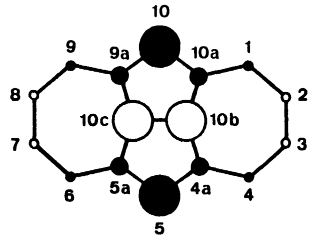
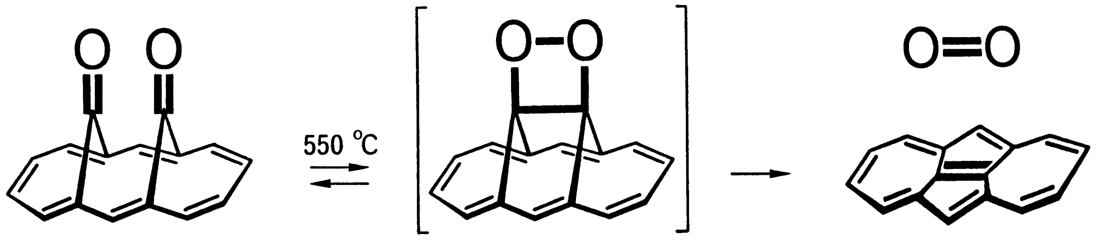


Fig. 1. HOMO of **1**.

Although **1** had originally been synthesized from *cis*-1,6:8,13-ethanediylidene[14]annulene[4b)] by dehydrogenation, it was the unprecedented thermal deoxygenation of 15,16-dioxo-*syn*-1,6:8,13-dimethano[14]annulene (**2**) by means of the metathesis reaction $\mathbf{2} \rightarrow \mathbf{3} \rightarrow \mathbf{1}$ [5)] - reversion of the well-known cleavage of suitably activated double bonds by singlet oxygen - that most conspicuously demonstrated the chemical relationship existing between bridged [14]annulenes and **1**. The intriguing question of whether or not the deoxygenation of **2** is a reversible process prompted us to explore the still virgin chemistry of **1** using theoretical considerations as a guide. In this communication some of the diverse oxidative transformations that **1** undergoes are reported.

Previous MO calculations on **1** [6)] employing the standard Hückel method showed the highest electron density to be at C5 and C10, and hence led to the prediction that electrophilic reagents should attack **1** preferentially at these centers. In fact, protonation[1a)] is found to occur at C5 affording a stable carbenium ion from which **1** can be regenerated on addition of water.

[#] Dedicated to Professor Teruaki Mukaiyama on the occasion of his 60th birthday.



2 **3** **1**

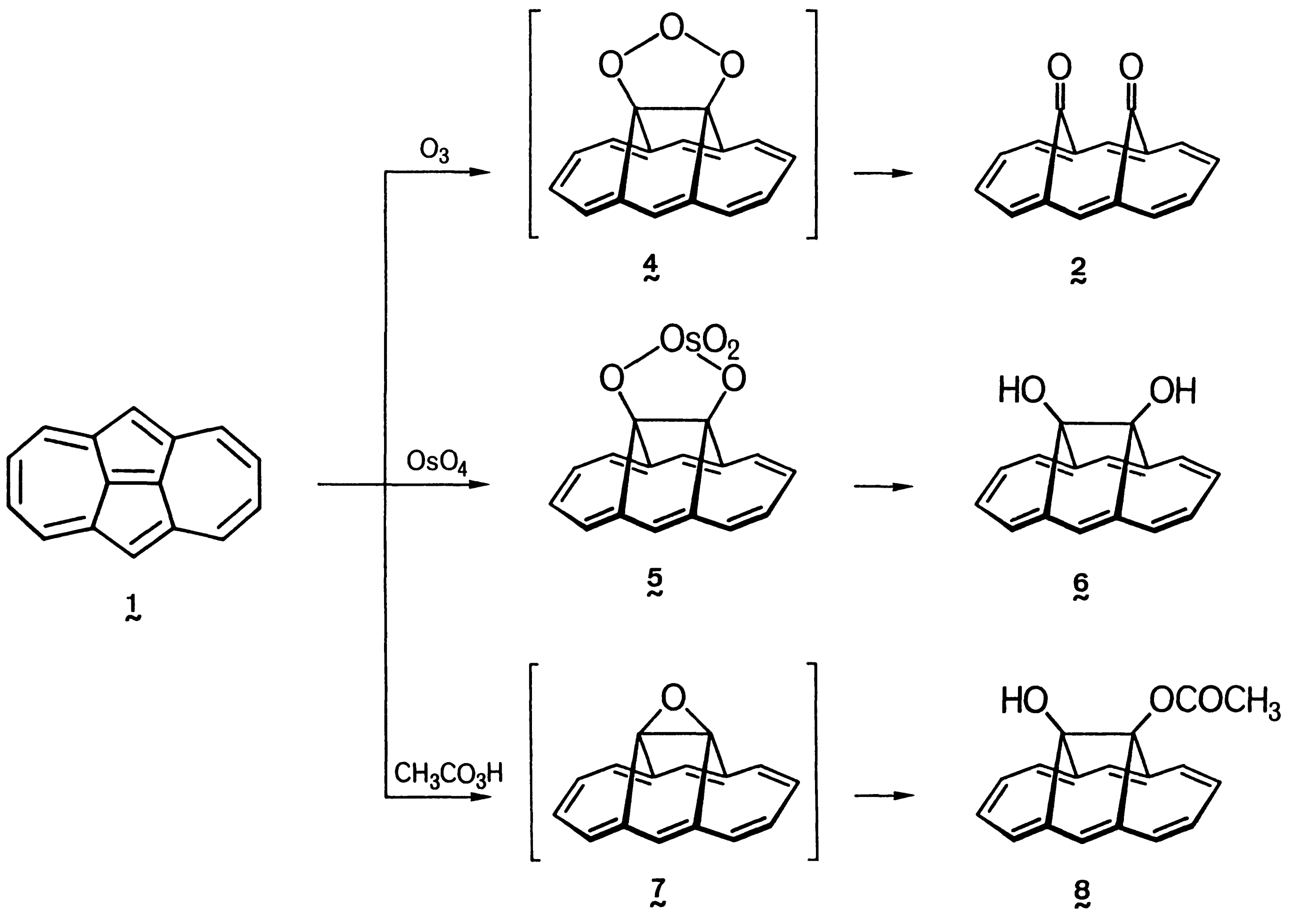
A clue as to how **1** would react with electrophilic reagents which - like singlet oxygen - are bidentate is provided by a consideration of the highest occupied molecular orbital (HOMO) of the hydrocarbon.[7] Regardless of whether the PPP[8a] approach, MINDO/3[8b] or MNDO[8c] methods were applied, one finds that the HOMO possesses significant orbital coefficients only at C5, C10, C10b, and C10c (Fig. 1). According to this picture, the reaction of **1** with a bidentate electrophile passing through a cyclic transition state or intermediate should occur at C10b and C10c since the interaction of the reagent with both 2p atomic orbitals at these centers will make two contributions of equal magnitude to the energy. If, on the other hand, such an electrophile attacks at C5 or C10 rather than at C10b and C10c, the gain in energy is halved because only one center participates in the bonding. The reaction of **1** with a monodentate electrophile at C10b or C10c requires a sizable localization energy in order to form the corresponding cationic species. However, due to the small coefficients at C4a/C5a and C9a/C10a, respectively, this is not the case if the reagent attacks at C5 or C10. The course of protonation of **1** is in agreement therewith.

The examination of the possibility that **1** on reaction with the bidentate electrophile singlet oxygen[9] would afford the diketone (**2**) via the dioxetane (**3**) has as yet failed to give conclusive results as **1** turned out to be more susceptible to attack by triplet than by singlet oxygen. When **1** is treated with singlet oxygen, generated either photochemically or by Foote's method, only 5,5'-bi(azuleno[2,1,8-ija]azulenyl), which is recognized as the product of oxidation of the hydrocarbon by triplet oxygen, could be isolated.[10]

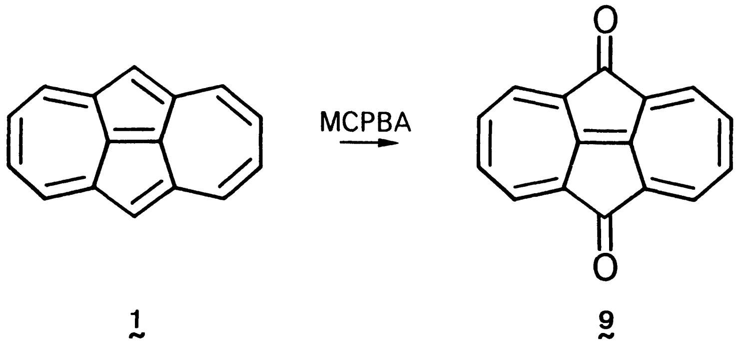
While addition to the central bond (C10b-C10c) of isopyrene (**1**) remains to be vindicated so far as singlet oxygen is concerned, this mode of reaction of **1** has since been dramatically verified by employing the bidentate oxidants ozone, osmium tetroxide, and peracetic acid. As inferred from the nature of the products isolated, these oxidations must involve **4**, **5**, and **7**, respectively, as the primary intermediate.

Ozonolysis of **1** in carbon tetrachloride/dichloromethane (2:1) in the presence of methanol at -78 °C, followed by reduction with dimethyl sulfide, led to a stable orange-colored diketone which, after chromatography (silicagel, dichloromethane) and crystallization (acetonitrile), proved to be identical in all respects with **2** (yield 40%). The competitive formation in minor amounts of the olefinic *anti*-isomer of **2**,[11] a molecule very prone to polymerize, cannot be rigorously excluded, but seems unlikely for mechanistic and steric grounds.

When an equimolecular amount of osmium tetroxide (in tetrahydrofuran) is added to a solution of **1** in hexane/pyridine (8:1) an apparently homogeneous cyclic osmate ester is obtained which on hydrolysis by aqueous potassium hydroxide in the presence of mannitol furnishes the *cis*-1,2-dihydroxy compound (**6**)[12] (yield 55%). Conversion of **1** into **6**, albeit in lower yield (15-20%), is also achieved by potassium permanganate oxidation employing phase transfer conditions. The structure of **6** is evident from the spectra and, moreover, follows from an X-ray investigation of the compound.



In the light of these findings, peracid oxidations of 1 promised to open an avenue to the *trans*-isomer of 6, a derivative of the as yet elusive *trans*-1,6:8,13-ethanediylidene[14]annulene. As it turned out, however, treatment of 1 with peracetic acid (100% excess) in dichloromethane in the presence of sodium acetate at 0 °C affords, after tedious chromatographic work-up, the 1,2-hydroxyacetate (8)[13] as the only isolable product (yield 12%). 8 is unequivocally shown to possess the *cis*-configuration by its virtually quantitative conversion into 6 by means of lithium aluminium hydride in ether. The epoxide (7) from which 8 must arise by a *cis*-opening of the epoxide ring induced by acetic acid has as yet defied all attempts of isolation. Actually, the pronounced tendency of 7 to react with acetic acid seems hardly surprising since ring opening of protonated 7 would lead to a carbenium ion that is appreciably stabilized by resonance. For steric and presumably also for thermodynamic reasons trapping of this ion by acetate can be anticipated to result in the formation of 8 rather than the corresponding *trans*-isomer.



Interestingly, the course of peracid oxidations of **1** markedly depends on reaction conditions. Thus, when **1** is oxidized with m-chloroperbenzoic acid (MCPBA) in ether at 0 °C, employing sodium bicarbonate as a buffer, the intriguing fulvenoid diketone (**9**) - whose formation bears a formal analogy to the oxidation of anthracene to anthraquinone - is obtained as the major product (ca. 20%). Isolation of **9** is facilitated, as the compound forms blue solutions (violet-black crystals with metallic luster) and is relatively polar. Evidence, based on spectral and structural findings, that **9** constitutes a resonance hybrid to which dipolar structures are the main contributors will be presented in a forthcoming publication.

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12) **6**: mp > 300 °C, orange-colored needles (chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 and 8.05 (AA'BB', H-2,5,9,12 and H-3,4,10,11, respectively, $J_{2,3}$ = 9.80 Hz, $J_{2,4}$ = 0.36, $J_{2,5}$ = 1.04, $J_{3,4}$ = 9.56), 8.29 (s, H-7,14), -0.55 (s, 2 H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 132.89, 132.37, 127.31, 123.36, 74.84; MS (70 eV): m/z 236 (M^+, 54%), 219 (33), 202 (100); UV/VIS (dioxane): λ_{max} = 300 nm (ε = 193000), 313 (43400), 352 (8500), 367 (8500), 382 (7100, sh), 440 (150), 510 (1700, sh), 550 (2000); IR (KBr): 3400 cm^{-1} (O-H).

13) **8**: mp 205-207 °C, orange-colored needles (dichloromethane/pentane); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36 and 8.00 (AA'BB', 4 H), 8.31 and 7.97 (AA'BB', 4 H), 8.21 (s, H-7,14), 1.11 (s, 3 H, CH_3), -0.46 (s, 1 H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 166.78, 131.87, 131.78, 127.24, 123.59, 122.95, 81.61, 75.52, 20.09; MS (70 eV): m/z 278 (M^+, 10%), 202 (54), 44 (100); UV/VIS (dioxane): λ_{max} = 297 nm (ε = 166000), 310 (39000, sh), 350 (7500), 365 (7700), 380 (6200, sh), 436 (200), 510 (1200); IR (CsI): 3436 cm^{-1} (O-H), 1724 (C=O).

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