was purified by column chromatography on silica gel/methylene chloride to give 77 mg (77%) of **15** as pale yellow crystals, mp 200–206 °C (recrystallized from ether/methanol): ^{1}H NMR ($CDCl_3$) δ 8.81 (d, J = 8.5 Hz, 1), 8.08 ("d", J = 7.2 Hz, 1), 7.72 (d, J = 8.2 Hz, 1), 7.63–7.57 (m, 1), 7.46–7.13 (m, 6), 6.92–6.86 (m, 1), 6.71–6.61 (m, 2), 6.26 (dd, J = 10.0, 2.6 Hz, Ha), 5.91 (dd, J = 10.0, 3.6 Hz, Hb), 4.42 (d, J = 3.0 Hz, He), 4.12 (d, J = 12.5 Hz, Hd), 3.28 ("dddd", J = 12.5, 3.6, 3.0, 2.6 Hz, Hc).

Photochemical Isomerization of Dianthrylpropanone 16 To Give 17. This reaction has been described in ref 19.

Acknowledgment. We are indebted to Mr. Gunnar Svensson for technical assistance.

Registry No. **1**, 1564-64-3; **2**, 54060-73-0; **3**, 84332-58-1; **4**, 4709-80-2; **5**, 102725-05-3; **6**, 88920-58-5; **7**, 77312-81-3; **8**, 68975-27-9; **9**, 102725-06-4; **10**, 102725-07-5; **11**, 102735-75-1; **12**, 102725-08-6; **13**, 102725-09-7; **14**, 102725-10-0; **15**, 102725-11-1; ethylene oxide, 75-21-8; Dess–Martin oxidant, 87413-09-0; 9-anthracenecarboxylic acid, 723-62-6; 9-anthryl chloride, 16331-52-5; anthracene, 120-12-7.

Dicyclopenta[*ef*,*kl*]heptalene (Azupyrene) Chemistry. Jutz Synthesis Byproducts. Synthesis and Thermal Isomerization of 1-Methylazupyrene[1]

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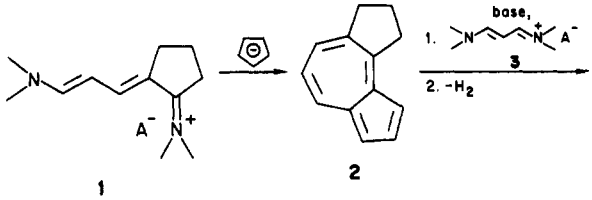
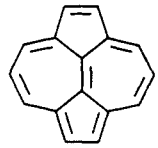
Received December 23, 1985

The Jutz synthesis of azupyrene (**4**) has been found to form chloro-, methyl-, and dimethylazupyrene byproducts in the final step. Perchlorate and methoxide ions were shown to cause the chlorination and methylation, respectively. Temperature control at 200–205 °C reduced the chlorination and the use of ethoxide virtually eliminated the alkylation. 1-Methylazupyrene (**7**) was synthesized. The thermal isomerization of **7** to methylpyrenes was carried out and the products were found to be those predicted by certain of the mechanisms proposed for the azulene to naphthalene isomerization.

After the first synthesis of dicyclopenta[*ef*,*kl*]heptalene (azupyrene, **4**) had established the stability and physical aromatic character of this 4n π electron structure,[3] a report by Jutz and Schweiger of a more direct route[4] contained a footnote which indicated a high yield conversion of 2,3-dihydro-1*H*-cyclopent[*e*]azulene (**2**) to **4**. Procedures for this latter route were then developed in our laboratories which closely approximated those subsequently reported[5] except that the tetrafluoroborate ion replaced perchlorate ion in the intermediate salt **1** and, initially, as the anion of the immonium reagent **3** for the formation of the second seven-membered ring (eq 1). The yield of **2** (31%) with



1 2



4 (1)

the tetrafluoroborate salt was satisfactory. However, the yield of **4** from **2** was quite low (≲12%)[6] compared to ca. 40–50% obtained with the perchlorate salt of **3**.

Scheme I

$$\text{dihydro-4} + ClO_4^- \rightarrow 4 + ClO_3^- + H_2O$$
$$\text{dihydro-4} + ClO_3^- \rightarrow 4 + HClO_2 + OH^-$$
$$\text{dihydro-4} + HClO_2 \rightarrow 4 + HClO + H_2O$$
$$4 + HClO \rightarrow \text{Cl-4} + H_2O$$

Although **4** as isolated melted sharply in the correct range, difficulties were encountered in obtaining analytically pure samples of derivatives subsequently prepared. High resolution GC/MS analysis showed that **2** was free of chlorination and methylation impurities but samples of **4** contained up to 4% methylazupyrene, 1% dimethylazupyrene, and up to 12% chloroazupyrene. The byproducts were therefore formed in the conversion of **2** to **4**. The azupyrene obtained when **3** (A = BF_4) was used contained no chloro impurities and the crude product had twice as much (ca. 40%) of the 1,2-dihydroazupyrene. The perchlorate ion was therefore the source of the chloro impurities and acted to oxidize 1,2-dihydroazupyrene to azupyrene. The reactions proposed for these processes are shown in Scheme I. Hypochlorite is a known reagent for the chlorination of aromatic compounds,[7] and it was shown that calcium hypochlorite effected the chlorination of **4**.

These findings led to further study of the conversion of **2** to **4**. Measurement of the evolution of dimethylamine (a product of each of two main steps involved in forming the new ring) showed that the alkylation of **2** by **3** occurred below 100 °C but that ring closure required ≳200 °C. The

(1) Presented in part at the 39th Northwest Regional Meeting of the American Chemical Society, Moscow, ID, June 13–15, 1984.

(2) Ph.D. Theses of Daugs, E. D., 1985; Kao, L. G., 1981, M.S. Thesis of Wang, J-F., 1976, University of Washington.

(3) Anderson, A. G., Jr.; MacDonald, A. A.; Montana, A. F. *J. Am. Chem. Soc.* **1968**, *90*, 2993. Anderson, A. G., Jr.; Masada, G. M.; Montana, A. F. *J. Org. Chem.* **1973**, *38*, 1439. Anderson, A. G., Jr.; Montana, A. F.; MacDonald, A. A.; Masada, G. M. *Ibid.* **1973**, *38*, 1445.

(4) Jutz, C. J.; Schweiger, E. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 808.

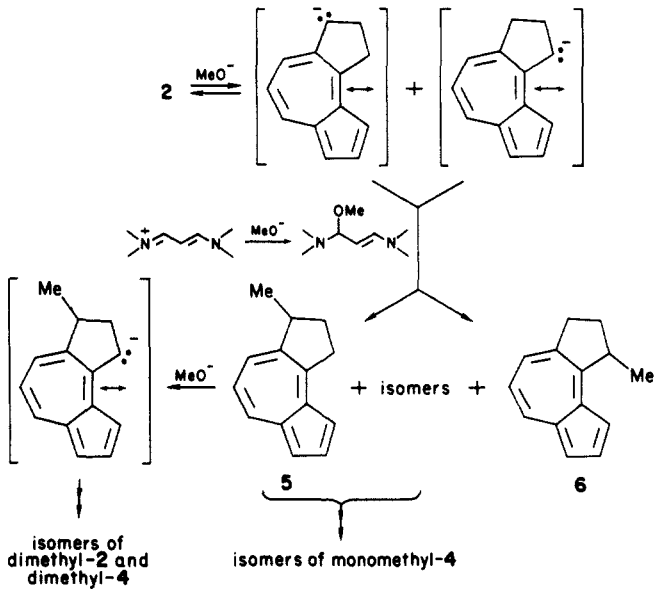
(5) Jutz, C. J.; Schweiger, E. *Synthesis* **1974**, 193. Prof. Jutz kindly provided some details prior to publication: personal communication, June 1973.

(6) The low yields from the BF_4^- salt were possibly due to the instability of the 1,2-dihydro-**4** which was shown (GC/MS) to be present early in the final heating in larger amounts (ca. 40%) in the absence of ClO_4^-. Prof. Jutz reported similar findings in analogous reactions to us: personal communication, Sept 1973.

(7) See: March, J. *Advanced Organic Chemistry*, 3rd ed.; John Wiley & Sons: New York, 1985; p 477.

0022-3263/86/1951-2961$01.50/0

Scheme II



amounts of chloro impurities were dependent on the temperature for the latter process, being 0.25–0.8% at 200–205 °C and up to 12% at 230 °C.[8] Quantities of <1% could be removed by flash chromatography so the lower temperature range is satisfactory.

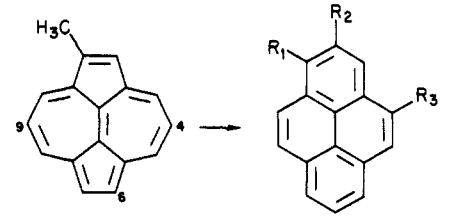
GC/MS analysis also revealed that the trimethyleneazulene (**2**) recovered from the reaction contained up to 22% methylated **2** and 17% dimethylated **2**. Thus, the recycling of this material (which had been done in some early runs) compounded the alkylation problem. The methylation of **2** and **4** by **3** was initially suspected, but the source of the methyl groups was shown to be the methoxide ion when the substitution of this by ethoxide (and ethanol) reduced the alkyl substitution impurities to ≲0.5%. A proposed scheme for the methylation of **2**, which would also lead to methyl derivatives of **4** is shown in Scheme II. Delocalization of the charge in the initial anion intermediates provides for the formation of the three possible methylazupyrene isomers, and analogous reaction of the intermediate **5** and its isomers would give the dimethyl products observed. The steric difference between methoxy and ethoxy in the proposed alkylating species formed is apparently sufficient to minimize the alkylation reaction. Intermediates having a methyl group located as in **6** are not able to react further to form derivatives of **4** and thus account in part for the presence of methylated **2** compounds in the product. The combination of the controlled, lower reaction temperature and the use of ethoxide/ethanol gave **4** of greater than 99% purity.

It was desired to synthesize 1-methylazupyrene (**7**) to have a derivative of known structure to confirm ^{1}H NMR assignments of electrophilic substitution products and to possibly provide information on the thermal isomerization to pyrene.[9] The first route explored was that of the Jutz synthesis with the substitution of 3-methylcyclopentanone for cyclopentanone. This work was performed prior to the above study on the formation of impurities, so the maximum final reaction temperature was 210 °C. The consequent difficult purification gave a low (7%) yield of **7**. The ^{1}H NMR spectrum of **7** provided confirmation of the spectral assignments for monosubstitution products.[10,11]

Subsequently, **7** was prepared in somewhat better (29%) yield from azupyrene via 1-[(dimethylamino)methyl]azupyrene by conversion to the quaternary salt and then hydride displacement (eq 2).

$$4 \xrightarrow[\text{HCHO, HOAc}]{(Me_2N)_2CH_2} 1\text{-}Me_2NCH_2\text{-}4 \xrightarrow[2.\ LiAlH_4]{1.\ MeI} 7 \qquad (2)$$

The thermal rearrangement of **4** to pyrene (**8**) (40%) was first carried out at 500–510 °C.[9] This reaction was subsequently found to be 90% complete (33% yield of **4** + **8**) after 6 h at 465–477 °C and 28% complete (90% yield of **4** + **8**) after 2 h at 450 °C. The synthesis of **7** provided the possibility of obtaining evidence concerning the pathway of this conversion. Heating **7** at 490–500 °C under N_2 formed **4** (67%), a mixture of monomethylpyrenes (24%), and unchanged **7** (9%) by GC/MS analysis (eq 3).



(3)

7

8, $R_1 = R_2 = R_3 = H$
9, $R_1 = CH_3$; $R_2 = R_3 = H$
10, $R_2 = CH_3$; $R_1 = R_3 = H$
11, $R_3 = CH_3$; $R_1 = R_2 = H$

Integration of the characteristic methyl singlets (δ 2.98, 2.80, and 2.90)[12] for **9**, **10**, and **11**, respectively, in the ^{1}H NMR spectrum gave a corresponding composition ratio of 23:23:4. The product of the same reaction at 450–460 °C contained **8** (39%), monomethylpyrenes (19%), **4** (39%), and unchanged **7** (3%) with a ratio of 25.5:20.5:4 for **9**, **10**, and **11**.

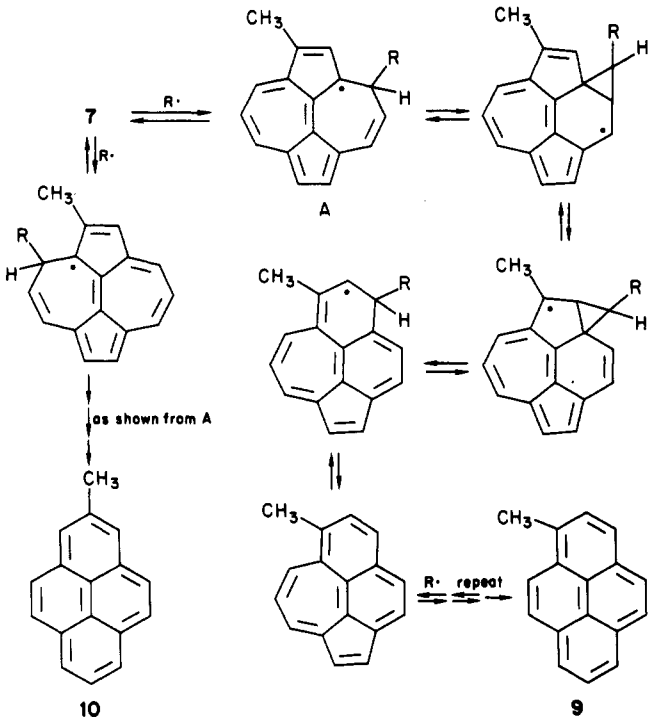
The thermal rearrangement of azulene to naphthalene has been the subject of numerous mechanistic studies.[13] No single mechanism can account for all of the products formed from ^{13}C-labeled azulene.[13-15] The majority of the products can be explained by concurrent norcaradiene–vinylidene[16] and radical initiated methylene walk[14] mechanisms, and the participation of the former seems well established. Other mechanisms which have been proposed involve (a) homolytic cleavage of the central C-9 to C-10 bond in azulene, a subsequent hydrogen shift, and carbon–carbon bond reformation (a diradical mechanism),[15] (b) two successive symmetry allowed pericyclic reactions (a bicyclobutane mechanism),[17] and (c) radical initiated formation of a spiro intermediate.[14] Two of these mechanisms are consistent with our results with **7** in that they predict the formation of essentially equal amounts of **9** and **10**: the methylene walk (Scheme III) wherein the radical initiation is presumed to have approximately equal probability of occurring at positions 3, 5, 8, or 10 on **7**, and the

(8) Jutz and Schweiger[5] reported a temperature range of 150–200 °C, at which negligible chlorination would be expected.

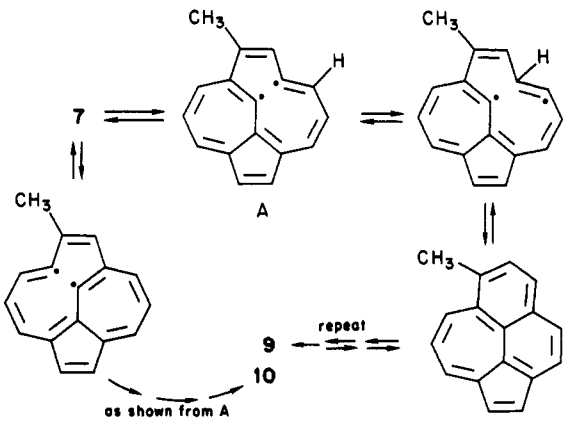
(9) For the preliminary report, see: Anderson, A. G., Jr.; Kao, L. G. *J. Org. Chem.* **1982**, *47*, 3589.

(10) Anderson, A. G., Jr.; Davidson, E. R.; Daugs, E. D.; Kao, L. G.; Lindquist, R. L.; Quenemoen, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 1896.
(11) Anderson, A. G., Jr.; Masada, G. M.; Kao, L. G. *J. Org. Chem.* **1980**, *45*, 1312.
(12) Keefer, L. K.; Wallcave, L.; Lou, J.; Peterson, R. S. *Anal. Chem.* **1971**, *43*, 1411.
(13) Zeller, K.-P. *J. Chem. Soc. Pak.* **1982**, *4*, 298. Scott, L. T. *Acc. Chem. Res.* **1982**, *15*, 22.
(14) Alder, R. W.; Wilshire, C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1464. Alder, R. W.; Whitesides, R. W.; Wittaker, G.; Wilshire, C. *J. Am. Chem. Soc.* **1979**, *101*, 629. Scott, L. T. *J. Org. Chem.* **1984**, *49*, 3021.
(15) Scott, L. T.; Kirms, M. A. *J. Am. Chem. Soc.* **1981**, *103*, 5875.
(16) Zeller, K.-P.; Wentrup, C. *Z. Naturforsch. B.* **1981**, *36b*, 852. Zeller, K.-P.; Wentrup, C.; Katz, E.; Becker, J. *J. Am. Chem. Soc.* **1980**, *102*, 5110.
(17) Scott, L. T.; Agopian, G. K. *J. Am. Chem. Soc.* **1977**, *99*, 4506.

Scheme III



Scheme IV

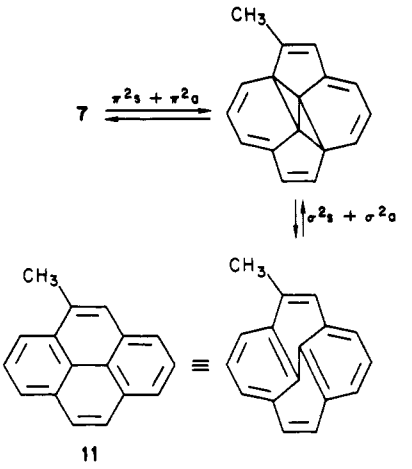


mechanistic process is repeated on the second azulene moiety and the diradical (Scheme IV) which would also involve the two azulenoid portions of **7** successively.

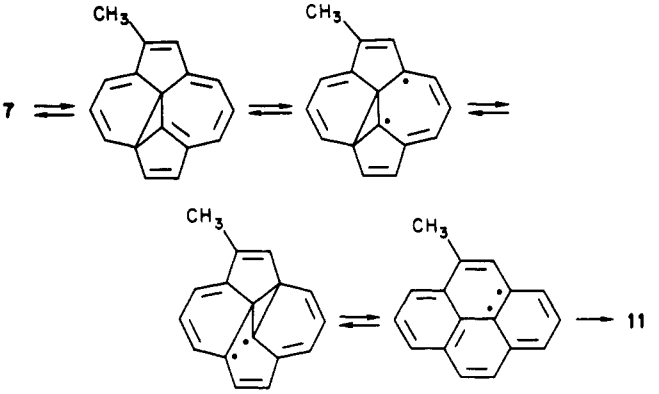
Two mechanisms, also, predict the formation of **11**: a bicyclo one (Scheme V) having symmetry allowed pericyclic reactions and a step-wise radical one involving a norcaradiene intermediate (Scheme VI).

The relatively large proportion of demethylation products raises the possibility of significant formation of **9**, **10**, and **11** via the methylation of pyrene (**8**). The mechanism for the thermal demethylation of methylazulenes during the rearrangement to naphthalenes has not been established, although evidence in support of a radical process has been obtained.[18] The methylation of **8** by methyl radicals would give a ca. 70:30 ratio of **9** to **10** and no **11**.[19] The formation of dimethylpyrene might also be expected but was not observed. Thus the experimental results are not consistent with a significant participation of methyl

Scheme V



Scheme VI



radicals in the formation of **9**, **10**, and **11**.

The preparation of 3,5-dimethylazupyrene, which would yield 3,5-dimethylpyrene as the sole product by the mechanisms of Schemes III and IV and 1,3-dimethylpyrene by the mechanisms of Schemes V and VI and thus provide confirmation of these processes, was attempted by the substitution of dimethyl[4-(dimethylamino)-3-pentenylidene]immonium perchlorate for the corresponding 2-propenylidene salt in the last ring-forming reaction of the synthesis (eq 1). Only a trace of the dimethylazupyrene was obtained. As for the azulene–naphthalene rearrangement, the synthesis of ^{13}C-labeled **7** (i.e., at C-1, and at C-3 plus C-5) should permit more definitive conclusions. We were not able to carry out these studies.

The possibility of thermal automerization, which was demonstrated for **8** at 1100 °C and shown not to occur via conversion to **4** by a methylene walk or diradical mechanism,[20] was examined under our reaction conditions. No **4** was detected to be formed from **8**.

Experimental Section

Equipment. NMR spectra were obtained with a Varian CFT-20, a Bruker CXP-200, or a Bruker WM 500 Cryospec spectrometer with Me_4Si as the internal standard. UV and visible spectra were recorded on a Hewlett-Packard 8450 A spectrophotometer with 1.0 or 0.1 cm quartz cells. Mass spectra were measured with a Hewlett-Packard 5985 GC/MS instrument with a 30 m (DB-5) fused silica capillary column. High resolution mass spectra were obtained on a V.G. Micromass 7070 H GC/MS and Associated V.G. 2035 F/B data system[21] with perfluorokerosene

(18) Alder, R. W.; Whitaker, G. *J. Chem. Soc., Perkin Trans. 2* **1975**, 714.

(19) Dickerman, S. C.; Feigenbaum, W. M.; Fryd, M.; Milstein, N.; Vermont, G. B.; Zimmerman, I.; McOmie, J. F. W. *J. Am. Chem. Soc.* **1973**, *95*, 4624.

(20) Scott, L. T.; Kirms, M. A.; Berg, A.; Hansen, P. E. *Tetrahedron Lett.* **1982**, *23*, 1859.

(21) Funding by NIH Biomedical Research Development Grant 1508 RR 09082 is gratefully acknowledged.

as the standard. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, or Canadian Microanalytical Service, Ltd., Vancouver, B. C. Melting points were taken with a Fischer Johns apparatus and are uncorrected.

Materials. Chemicals were reagent grade and further purified when so indicated. Tank N_2 or Ar as passed through concentrated H_2SO_4, over Na_2SO_4 or $CaCl_2$ and then over NaOH pellets, and, finally, over reduced BTS (BASF Cu·Al_2O_3) catalyst. $CHCl_3$ and CH_2Cl_2 were dried over $CaCl_2$ and distilled from P_2O_5. Quinoline was stored over KOH pellets and distilled at 1.5 torr prior to use. *n*-Hexane and mixed hexanes were shaken with a mixture of concentrated H_2SO_4 and HNO_3, washed successively with H_2O, aqueous $NaHCO_3$, and H_2O, dried (Na_2SO_4), distilled, and passed through a 4 in. × 1 in. column of acidic Al_2O_3. Ether and THF were dried (Na_2SO_4), refluxed with Na and benzophenone until a blue color formed, and distilled. Pyridine was dried over KOH pellets and distilled from CaO. 1,4-Dioxane was refluxed overnight with 1.5 N hydrochloric acid with a slow N_2 flush, dried (twice) over KOH pellets, refluxed overnight over Na (N_2 atmosphere), and then distilled and stored under N_2. Benzene was shaken with concentrated H_2SO_4 to a clear acid layer, washed with H_2O and 10% $NaHCO_3$, dried (Na_2SO_4), and distilled by using a Dean–Starke trap to separate the initial cloudy fraction. Acetic acid was distilled from P_2O_5. Chloranil was recrystallized from ethanol. Gravity chromatography columns were prepared with layers of sand above and below the Al_2O_3 (ca. 150 mesh) or Merck silica gel grade 60, 100–200 mesh. Flash chromatography columns were prepared with Merck silica gel grade 60, 230–400 mesh. Precoated TLC plates were obtained from MCB Manufacturing Chemists, Inc., Cincinnati, OH. Analytical plates (0.25 mm) and preparative plates (2 mm) were prepared with silica gel 60 F-254. Plates with colorless products were visualized with UV light or I_2 vapor.

2,3-Dihydro-1*H*-cyclopent[*e*]azulene (2). The procedure used was similar to that described by Jutz and Schweiger.[5] All solvents, reagents, and gases were anhydrous and deoxygenated. All glassware was dried under Ar. Sodium cyclopentadienide was prepared with stirring and cooling in a three-necked, 250-mL flask fitted with a condenser, addition funnel, and gas inlet and having an additional outlet tube below the center which was connected via a stopcock to a three-necked, 1-L flask fitted with a condenser in gas inlet. A solution of the product from 2.9 g (0.12 mol) of NaH and 10 mL (0.12 mol) of freshly formed, distilled and dried (Na_2SO_4) cyclopentadiene in 120 mL of tetrahydrofuran was added slowly, with stirring, to a solution of 23.3 g (0.083 mol) of **1** (A = BF_4, mp 181–182 °C)[5] in 120 mL of pyridine under Ar in the 1-L flask. Stirring was continued for 6–8 h and the mixture then heated under reflux for 12–16 h. The solvents were removed under vacuum from the cooled mixture and the semisolid residue was refluxed with 500 mL of 30–60 °C petroleum ether for 1 h. The cooled extract was filtered through Celite, and the volume was reduced to 300 mL before a second filtration through a 1 × 1.5 in. silica gel column and washing with 200-mL portions of 1 N hydrochloric acid until the organic layer was clear, then H_2O (3 × 200 mL), and 10% $NaHCO_3$. Removal of the solvent from the dried (Na_2SO_4) solution and chromatography of the residue over neutral Al_2O_3 (hexanes as the eluent) gave 2.46–4.2 g (18–31%) of **2** as a blue oil: UV–vis (hexanes) λ_{max} 246 nm (log ϵ 4.34), 275 (sh, 4.56), 280 (4.61), 283 (sh, 4.58), 316 (3.27), 323 (3.37), 328 (3.46), 338 (3.58), 343 (3.63), 354 (3.15), 362 (2.32), 484 (sh, 1.85), 532 (sh, 2.38), 554 (2.52), 578 (2.63), 600 (2.60), 630 (2.63), 656 (2.42), 694 (2.34); ^{1}H NMR ($CDCl_3$) δ 2.20 (p, 2, H-2′, J = 7.2 Hz), 3.23 (t, 2, H-3′, J = 7.2 Hz), 3.52 (t, 2, H-1′, J = 7.2 Hz), 7.06 (t, 1, H-7, J = 9.5 Hz), 7.21 (d, 1, H-3, J = 3.8 Hz), 7.27 (d, 1, H-1, J = 3.8 Hz), 7.61 (d, 1, H-6, J = 9.5 Hz), 7.81 (t, 1, H-2, J = 3.8 Hz), 8.26 (d, 1, H-8, J = 9.5 Hz); mass spectrum, m/e (relative intensity) 169 (14), 168 (M^+, 100), 167 (54), 166 (15), 165 (40), 153 (15), 152 (30); exact mass, m/e 168.0939 ($C_{13}H_{12}$ requires 168.0939).

Dimethyl[3-(dimethylamino)-2-propenylidene]immonium Perchlorate and Tetrafluoroborate (3). The procedure of Malhorta and Whiting[22] was modified by the substitution of benzene (50 mL) to cover the dimethylammonium perchlorate obtained from 24 mL of 70% $HClO_4$ (0.266 mol) and 75 mL of 20% aqueous dimethylamine (0.30 mol) and (100 mL) as the solvent for the dropwise addition of 24.4 g (0.246 mol) of 3-(dimethylamino)propenal. The mixture was refluxed for 3 h by using a Dean–Starke trap to remove the H_2O formed. The precipitate which formed on overnight refrigeration was separated, recrystallized from ethanol, and vacuum dried to give 31.8 g (58%) of light yellow needles, mp 117–119 °C (lit.[22] mp 120 °C).

Repetition of the procedure using dimethylammonium tetrafluoroborate gave 56% of the corresponding salt as yellow orange needles, mp 112–114 °C: ^{1}H NMR ($CDCl_3$) δ 3.10 (s, 6, CH_3), 3.32 (s, 6, CH_3), 5.12 (t, 1, H-2), 7.72 (d, 2, H-1,3).

Dicyclopenta[*ef*,*kl*]heptalene (Azupyrene) (4). The procedure of Jutz and Schweiger[5] employing 3.7 g (16.3 mmol) of **3** (A = ClO_4) and 1.03 g (6.11 mmol) of **2** was modified as follows. A dry oxygen-free Ar atmosphere was maintained by a positive pressure of the gas and the outlet gas, after passing through a West condenser topped by a Graham condenser, was bubbled into 1.0 L of aqueous hydrochloric acid (pH 1.8–2.0). All reagents and glassware were anhydrous and solvents were also deoxygenated (Ar flushing after distillation). Sodium ethoxide (prepared fresh from Na and absolute ethanol) and ethanol were substituted for sodium methoxide and methanol. The progress of the reaction was monitored by the amount of dimethylamine produced as shown by the pH change of the acid solution from, for example, 1.93 to 2.18 after 18 h at 140 °C. This corresponded to 5.09 mmol of dimethylamine (0.82 equiv). Then the pH reached a value of 2.61 after ca. 9 h at 200–204 °C, indicating 9.25 mmol (1.5 equiv) of dimethylamine. Essentially no dimethylamine was evolved below 140 °C. The reaction could also be monitored by TLC: a blue spot, R_f 0.41, for **2** and a yellow spot, R_f 0.12, for **4**. After removal of the solvents under vacuum (1.5 torr), the residue was refluxed with 50 mL of CH_2Cl_2, then mixed with 20 g of neutral Al_2O_3, and the whole placed in a Soxhlet thimble and extracted with CH_2Cl_2 until the extract was essentially colorless. The 2 N hydrochloric acid and H_2O washes of the extract were followed by a 10% $NaHCO_3$ wash. Chromatography of the residue from the dried (Na_2SO_4) solution on neutral Al_2O_3 and elution with benzene gave a mixture of ca. equal amounts of **2** and then a mixture (5:1) of **4** and its 1,2-dihydro derivative (GC/MS analysis). After treatment with chloranil (1.5 g, 6.1 mmol) and workup, 0.363 g (35%) of unchanged **2** and 0.52 g (42%, 65% net) of crude **4**, mp 260–261 °C (lit.[5] mp 257–259 °C), were obtained. GC/MS analysis of the crude **4** showed the presence of ca. 0.5% chloro (m/e at 236 and 238), 0.2% methyl (m/e at 216), and 0.3% dimethyl (m/e at 230) derivatives.

The same procedure with 0.893 g (5.3 mmol) of **2** and 2.93 g (13.7 mmol) of **3** (A = BF_4) gave 0.13 g (12%, 15% net) of **4** which was free of chlorine containing impurities.

The use of sodium methoxide and methanol and **3** (A = ClO_4) with a final reaction temperature of 210 °C gave a 32% yield of **4** which contained ca. 5% chloro, 4% methyl, and 1% dimethyl derivatives (CG/MS analysis). The recovered material containing **2** (up to 40%) also consisted of up to 22% monomethyl and 17% dimethyl derivative of **2**. If the final reaction temperature was 230 °C, the yield of **4** was 31% including ca. 12% chloroazupyrene.

Reaction of 4 with Hypochlorite. The method was adapted from that of Hedge and Wolinsky.[23] To a solution of 8.5 mg (0.042 mmol) of **4** in 10 mL of CH_2Cl_2 was added, with stirring, a solution of 6.0 mg (0.042 mmol) of $Ca(OCl)_2$ in 1 mL of H_2O. Small pieces of solid CO_2 were added and the reaction monitored by TLC: R_f 0.74 (**4**), 0.80 (Cl-**4**), and 0.83 (di-Cl-**4**).[24] After 30 min, the mixture was washed with 10% $NaHCO_3$ and dried (Na_2SO_4) and the solvent was removed; GC/MS analysis of the product (11 mg) showed the presence of 24% unchanged **4**, 60% chloro-**4**, and 16% dichloro-**4**. Flash chromatography (20 × 1 in, silica gel column, CCl_4) gave 4.0 mg of a chlorine-rich fraction (87% mono-Cl, 12% di-Cl by GC/MS) the ^{1}H NMR spectrum of which indicated a 3:2 ratio of 1-chloro to 4-chloro derivatives of **4** [1-chloro, δ 7.34 (t, 1, H-4, J = 9.5 Hz), 7.39 (t, 1, H-9, J = 9.5 Hz), 8.30 (s, 1, H-2), 8.35 (d, 1, H-6, J = 4.5 Hz), 8.39 (d, 1, H-7, J = 4.5 Hz), 8.54 (d, 1, H-5, J = 9.5 Hz), 8.63 (d, 1, H-3, J = 9.5 Hz), 8.67 (d, 1, H-8, J = 9.5 Hz), 8.72 (d, 1, H-10, J = 9.5 Hz); 4-chloro, δ 7.36 (t, 1, H-9, J = 9.5 Hz), 8.30 (d, 2, H-2,6, J = 4.5 Hz), 8.40 (d, 2, H-1,7, J = 4.5 Hz), 8.67 (d, 2, H-8,10, J = 9.5 Hz), 8.75 (s, 2, H-3,5);

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UV–vis (hexanes) λ_{max} 266 nm (log ϵ 4.90), 287 (4.42), 301 (4.35), 312 (4.35), 336 (4.05), 3.46 (4.21), 359 (3.54), 410 (3.07), 444 (3.15), 460 (4.20), 486 (3.82), 492 (3.86)] corresponding to that of the product mixture from the reaction of **4** with Cl_2.[24]

1-[(Dimethylamino)methyl]azupyrene. The procedure was adapted from that of Lindsay and Hauser.[25] A 0.5-mL portion (0.5 mmol of reagent) of a clear solution formed by heating (steam bath) 30 mg (1.0 mmol) of paraformaldehyde and 0.15 mL (1.1 mmol) of tetramethyldiaminomethane in 2.0 mL of acetic acid was added to 52.5 mg (0.26 mmol) of **4** suspended in 6.0 mL of acetic acid. As the mixture was warmed to 70–80 °C, **4** dissolved and the solution became green. After 2 h, the mixture was cooled, diluted with 50 mL of H_2O, and extracted with 3 × 20-mL portions of ether. The extracts yielded 10 mg (20%) of unchanged **4**. The cooled (ice bath) aqueous solution was basified (1 N NaOH) and then extracted with ether. Removal of the solvent from the combined, dried (Na_2SO_4) extracts gave 47 mg (70%, 86% net) of 1-[(dimethylamino)methyl]azupyrene as a green solid which decomposed on standing: UV–visible (hexanes) λ_{max} 254 nm (log ϵ 4.40), 267 (4.59), 287 (4.22), 302 (4.00), 312 (3.98), 336 (3.68), 347 (3.74), 359 (3.26), 408 (2.70), 442 (2.85), 452 (2.90), 460 (2.78), 472 (3.15), 484 (3.69); ^1H NMR ($CDCl_3$) δ 2.4 (s, 6, CH_3), 4.3 (s, 2, CH_2), 7.35 (t, 1, H-4, J = 9.5 Hz), 7.40 (t, 1, H-9, J = 9.5 Hz), 8.37 (s, 1, H-2), 8.39 (d, 1, H-6, J = 4.3 Hz), 8.41 (d, 1, H-7, J = 4.3 Hz), 8.64 (d, 1, H-3, J = 9.5 Hz), 8.67 (d, 1, H-5, J = 9.5 Hz), 8.71 (d, 1, H-8, J = 9.5 Hz), 8.86 (d, 1, H-10, J = 9.5 Hz); mass spectrum, m/e (relative intensity) 259 (M^+, 30), 216 (35), 215 (100); exact mass, m/e 259.1378 ($C_{19}H_{17}N$ requires 259.1361).

1-Methylazupyrene (7). A. From 3-Methylcyclopentanone. The procedure indicated for the preparation of **4** was repeated with the substitution of 3-methylcyclopentanone for cyclopentanone. The final product (**7**) was obtained as gold-green leaflets (7% overall), mp 134–135 °C: UV–vis (hexanes) λ_{max} 254 nm (log ϵ 4.30), 267 (4.55), 287 (4.14), 302 (3.90), 312 (3.88), 334 (3.56), 347 (3.68), 359 (3.14), 410 (2.55), 442 (2.71), 452 (2.78), 460 (2.68), 472 (3.01), 484 (3.60); ^1H NMR ($CDCl_3$) δ 3.07 (s, 3, CH_3), 7.34 (t, 1, H-4, J = 9.5 Hz), 7.36 (t, 1, H-9, J = 9.5 Hz), 8.24 (s, 1, H-2), 8.39 (d, 1, H-6, J = 4.5 Hz), 8.42 (d, 1, H-7, J = 4.5 Hz), 8.55 (d, 1, H-10, J = 9.5 Hz), 8.58 (d, 1, H-3, J = 9.5 Hz), 8.65 (d, 1, H-5, J = 9.5 Hz), 8.70 (d, 1, H-8, J = 9.5 Hz); mass spectrum, m/e (relative intensity) 215 (29), 216 (M^+, 50), 217 (9); exact mass, m/e 216.0937 ($C_{17}H_{12}$ requires 216.0939). Anal. Calcd for $C_{17}H_{12}$: C, 94.41; H, 5.59. Found: C, 94.41; H, 5.66.

B. From 1-[(Dimethylamino)methyl]azupyrene. To a solution of 28.5 mg (0.11 mmol) of 1-[(dimethylamino)methyl]-azupyrene in 5 mL of CH_2Cl_2 was added 0.1 mL (1.1 mmol) of CH_3I. The mixture was stirred in the capped flask for 1 h and then placed in a refrigerator overnight. Collection of the green precipitate yielded 38.0 mg (85%) of product presumed to be (1-azupyrenylmethyl)trimethylammonium iodide, mp 222–225 °C dec: UV–vis (EtOH) λ_{max} 252 nm (log ϵ 4.72), 266 (4.90), 287 (4.47), 300 (4.32), 309 (4.26), 336 (4.00), 344 (3.85), 361 (3.64), 440 (3.00), 452 (3.11), 472 (3.45), 484 (4.10); ^1H NMR (Me_2SO-d_6) δ 3.30 (s, 9, CH_3), 5.48 (s, 2, CH_2), 7.51 (t, 1, H-4, J = 9.5 Hz), 7.58 (t, 1, H-9, J = 9.5 Hz), 8.60 (s, 2, H-6,7), 8.82 (s, 1, H-2), 8.89 (d, 1, H-8, J = 9.5 Hz), 8.92 (d, 2, H-3,5, H-3,5, J = 9.5 Hz), 9.13 (d, 1, H-10, J = 9.5 Hz).

A mixture of 29.2 mg (0.0728 mmol) of the above quaternary salt and 4.0 mg (0.106 mmol) of $LiAlH_4$ in 4.0 mL of freshly distilled dioxane was warmed (oil bath) to 50 °C under Ar in a flame-dried flask. After 2 h, the solid had dissolved to form a green solution and TLC (CH_2Cl_2) showed no immobile reagents. The cooled reaction was quenched with a few drops of H_2O and the mixture was added to 10 mL of H_2O. The whole was extracted with ether (3 × 10 mL) and the organic extracts were washed with 20-mL portions of 1 N hydrochloric acid and 10% $NaHCO_3$. The solvent was removed from the dried (Na_2SO_4) organic phase and the residue chromatographed (3 × 0.5 in silica gel column, hexanes) to give 7.5 mg (48%) of **7**, mp 132–133 °C, after sublimation at 150 °C and 0.1 torr, spectrally identical (UV–vis, ^1H NMR, mass spectrum) with the material from A.

Thermal Isomerization of Azupyrene (4).[9] In a 5-mL, thick-walled Vycor tube sealed under dry N_2 at 10^{-4} torr, 5 mg (0.025 mmol) of **4** was heated at 500 °C for 12 h. The cooled solid product was extracted with $HCCl_3$ to give 2 mg (40%) of pyrene (**8**) (no unchanged **4**) identical (mass spectrum, fluorescence spectrum[26]) with an authentic sample.

Repetition of the reaction at 450 °C for 2 h gave 4.5 mg of a mixture of **8** (25.2%) and unchanged **4** (64.8%) as indicated by the ^1H NMR spectrum: ($CDCl_3$) δ 8.00 (t, 2, H-2,7, J = 7.5 Hz), 8.08 (s, 4, H-4,5,9,10), 8.19 (d, 4, H-1,3,6,8, J = 7.5 Hz) for pyrene and 7.37 (t, 2, H-4,9, J = 9.5 Hz), 8.42 (s, 4, H-1,2,6,7), 8.71 (d, 4, H-3,5,8,10, J = 9.5 Hz) for **4**.[3]

Thermal Isomerization of 1-Methylazupyrene (7). In the manner described for the isomerization of **4**, a 3.5 mg (0.016 mmol) sample of sublimed **7** was heated at 500 °C and 0.2 torr to give 2.3 mg of a mixture containing (GC/MS analysis) pyrene (**8**) (67%), methylpyrenes (24%), and **7** (9%). Integration of the intensities of the methyl group singlets in the ^1H NMR spectrum ($CDCl_3$ at δ 2.98, 2.80, and 2.90, respectively,[12] showed a ratio of 23:23:4 for 1- (**9**), 2- (**10**), and 4-methylpyrene (**11**)).

The same reaction with 4.5 mg (2.1 mmol) of **7** at 450–460 °C for 4 h gave 2.1 mg which contained (GC/MS analysis) **8** (39%), methylpyrenes (19%), **4**(39%), and **7**(3%). The ^1H NMR spectrum showed a ratio of 25.5:20.5:4 for **9**, **10**, and **11**.

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Micellar Catalysis of Organic Reactions. 18. Basic Hydrolysis of Diazepam and Some N-Alkyl Derivatives of Nitrazepam

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Kinetic and mechanistic studies of the basic hydrolysis of several benzodiazepinone drugs have been carried out in the presence of micelles of cetyltrimethylammonium bromide (CTAB) and in aqueous solution. For diazepam, a change of mechanism from initial azomethine hydrolysis in water to initial amide hydrolysis in the presence of micelles of CTAB is indicated. For nimetazepam and *N*-benzylnitrazepam, initial amide hydrolysis was observed both in the presence of CTAB and in water. For the latter compounds, strong catalysis (50–100) of amide hydrolysis (phase 1) by micelles of CTAB was observed, while azomethine hydrolysis (phase 2) was only very weakly catalyzed (3–4-fold). For diazepam, the catalysis was smaller (9–18-fold), but this was accompanied by a mechanistic change so that here the actual catalysis of amide hydrolysis is masked.

The benzodiazepinones **1** are a class of physiologically active drugs, which include diazepam (**1a**) and nitrazepam (**1b**). These drugs are valuable because of their anxiolytic, anticonvulsant, and muscle relaxant properties.[1]

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