The reason for the difference in response to substituents is probably found in the geometries of the *n*-butyl and *tert*-butyl compounds (Table III). In the *tert*-butyl series, the C–C–X bond angles to the substituents is smaller than for the *n*-butyl series, and this results from the repulsion between the three methyl groups in the former. A smaller C–C–X angle implies greater ρ orbital character in the C–X bond. Since electronegative substituents prefer an orbital with high p character[9] they will prefer to be bonded to a *tert*-butyl group rather than *n*-butyl.

Calculations

The ab initio calculations were carried out using GAUSSIAN-86,[10] and the analysis of the wave functions was carried out using PROAIMS.[11]

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The Thermal Isomerization of [2a,11-$^{13}C_2$]Dicyclopenta[*ef*,*kl*]heptalene (Azupyrene) to Pyrene

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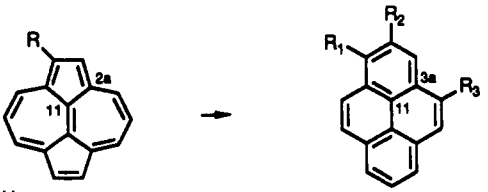
[2a,11-$^{13}C_2$]Dicyclopenta[*ef*,*kl*]heptalene (azupyrene) has been synthesized from [1,2-$^{13}C_2$]cyclopentanone which, in turn, was prepared from ^{13}C-labeled cyanide and ^{13}C-labeled iodomethane. Thermal isomerization of the labeled azupyrene gave [3a,11-$^{13}C_2$]pyrene. The only proposed mechanisms consistent with this result are the radical-initiated methylene walk and that involving a peripheral bicyclobutane intermediate. These mechanisms are also in agreement with previous results from the isomerization of 1-methylazupyrene except for an additional minor product in the latter experiment. Evidence for the automerization of pyrene under the thermal isomerization conditions has been obtained.

In an earlier study[2] of the thermal isomerization of azupyrene (**1**) to pyrene (**2**) the isomerization of 1-methylazupyrene (**3**) (eq 1) was found to give 1-methylpyrene (**4**), 2-methylpyrene (**5**), and 4-methylpyrene (**6**) in a ratio of 25.5:20.5:5.4. Two of five mechanisms which had



(1)

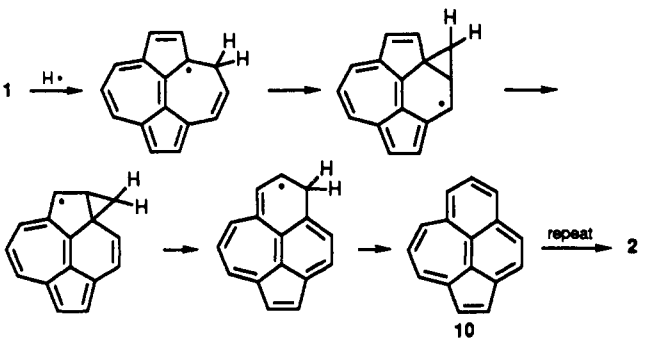
1: R = H
3: R = CH_3
7: R = H; C–2a = C–11 = ^{13}C

2: $R_1 = 2_2 = R_3$ = H
4: $R_1 = CH_3$; $R_2 = R_3$ = H
5: $R_2 = CH_3$; $R_1 = R_3$ = H
6: $R_3 = CH_3$; $R_1 = R_2$ = H
9: $R_1 = R_2 = R_3$ = H; C–3a = C–11 = ^{13}C

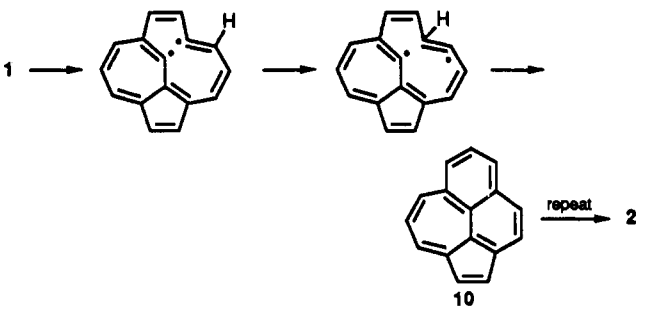
been proposed[3] for the thermal isomerization of azulene to naphthalene, the radical-initiated methylene walk (Scheme I) and one initiated by homolysis of a peripheral bridgehead–central carbon bond (Scheme II), were consistent with the formation of approximately equal amounts of **4** and **5**. Two other mechanisms, one involving formation of an internal bicyclobutane through symmetry-allowed pericyclic reactions and a stepwise radical process involving a norcaradiene structure, could account for the formation of **6**. At that time the desirability of carrying out the isomerization on ^{13}C-labeled azupyrene was noted. The synthesis of [2a,11-$^{13}C_2$]azupyrene (**7**) and the rearrangement of this to ^{13}C-labeled pyrene are now reported.

The methylene walk and the bridgehead–central carbon bond homolysis mechanisms differ in that the bond

Scheme I



Scheme II



cleavage in the latter leads to the separation in the product of the two carbons whereas in the former these carbons remain at the corresponding positions in the product. As these were the mechanisms of major concern, **7**, with adjacent, labeled bridgehead and central carbons, was selected for synthesis.

The incorporation of [1,2-$^{13}C_2$]cyclopentanone (**8**) in the Jutz synthesis[4] would give **7**, and **8** was prepared in 17% overall yield by the route shown (eq 2). The displacement

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(3) Scott, L. T. *Acc. Chem. Res.* **1982**, *15*, 22.
(4) Jutz, C. J.; Schweiger, E. *Synthesis* **1974**, 193.

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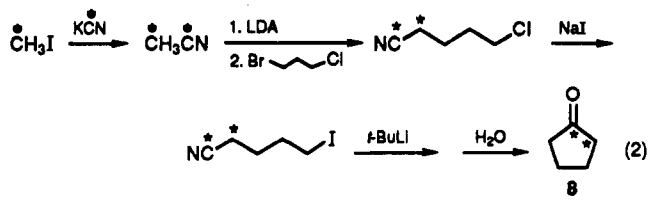
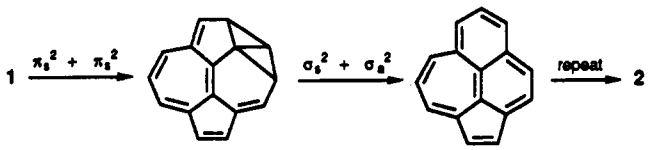


of bromide from 1-bromo-3-chloropropane was very selective, and in most runs none of the alternative bromopentanenitrile product was observed. For the ring closure, *tert*-butyllithium was much superior to other reagents (e.g. *n*-butyllithium, lithium, magnesium) tried.

Incorporation of diluted (to 18% ^{13}C enrichment), dilabeled cyclopentanone in the Jutz synthesis, with further dilution (to 1.94% ^{13}C enrichment) of the intermediate 4,5-trimethyleneazulene, gave [2a,11-$^{13}C_2$]azupyrene (**7**). The isotopic enrichment in **7** was determined by comparison of the average of the intensities of the two sets of doublet peaks from the adjacent ^{13}C carbons to those of the corresponding singlet peaks from the natural abundance compound to be 1.92%. One improvement was made in the synthetic scheme: 3-(dimethylamino)propenal was prepared in one operation from propargyl alcohol, manganese dioxide, and dimethylamine in 32% yield using the procedure described by Makin.[5] The ^{13}C NMR spectra of the labeled intermediates *N*-cyclopentylidenedimethylammonium fluoroborate, dimethyl[5-(dimethylamino)-1,2-trimethylenepentadien-2,4-ylidene]ammonium fluoroborate, and 4,5-trimethyleneazulene were recorded.[1]

The thermal isomerization of **7** gave pyrene which was 1.17% ^{13}C enriched in the 3a- and 11-positions (**9**). The ^{13}C NMR peak ratios of the other carbons corresponded to those in the spectrum of natural pyrene, indicating that the remaining 0.75% of ^{13}C enrichment was equally distributed among these other carbons. The retention of enrichment in the adjacent bridgehead and central carbons shows that the bond joining these is not broken in the principal mechanism(s) of pyrene formation. The heats of formation for azupyrene (113.5 kcal/mol, azuleno[3,3a,4,5-*cde*]naphthalene (**10**) (a proposed intermediate) (90.5 kcal/mol), and pyrene (60.4 kcal/mol) were calculated,[6] and the values obtained make ^{13}C scrambling at ca. 450 °C by a reverse isomerization involving **10** (via successive cleavage of two nonadjacent bridgehead-central carbon bonds) unlikely. Scott[7] has reported carbon scrambling (automerization) in pyrene in 2 s at 1100 °C. Thus pyrene and/or azupyrene might undergo this process at 450 °C over the 5–6-h period of our experiment after and/or before the isomerization occurs. To test the first possibility, a sample of the [3a,11-$^{13}C_2$]pyrene was heated at 450 °C for 5.5 h. At the end of this time the ^{13}C NMR spectrum of the sample closely matched, peak for peak, that of natural ^{13}C abundance pyrene. Thus complete scrambling had occurred. It seems probable that the less stable azupyrene would behave similarly and the automerization process is therefore proposed to account for the "disappearance" of 0.75% of the labeling during the isomerization despite the fact that the mechanism involved must involve interchange of the central and peripheral carbons, a process not included in any of the proposed isomerization mechanisms. Of the proposed isomerization mechanisms, only the methylene walk (Scheme I) and a peripheral bicyclobutane one[3] (Scheme III) give pyrene exclusively ^{13}C enriched at the 3a- and 11-positions and also 1- and 2-methylpyrene (**4** and **5**) from 1-methylpyrene (**3**). Thus the presence of the alkyl group in **3** must increase the relative rate of one or more other mechanisms (e.g. the internal bicyclobutane and the radical norcaradiene) such that a small amount of 4-methylpyrene (**6**) is formed.

Scheme III



Experimental Section

General. Chemicals were reagent grade and not further purified unless otherwise specified. N_2 and Ar were purified by passage over Drierite, then through a 38 cm column of reduced BTS (BASF Cu·Al_2O_3) catalyst at 180 °C, and then over KOH plus Drierite. Recrystallization and chromatography solvents were Baker reagent grade or Omnisolve. Pure, dry solvents were obtained as follows. Benzene was shaken with concentrated H_2SO_4 to a clear acid layer, washed with H_2O then 10% $NaHCO_3$, dried ($MgSO_4$), and distilled (Dean–Stark trap to remove wet forerun). Hexanes and pentane were shaken with a H_2SO_4–HNO_3 mixture, washed with H_2O then 10% $NaHCO_3$, dried ($MgSO_4$), distilled, and then passed through a 10 × 2.5 cm column of acidic Al_2O_3. Halomethanes were distilled from P_2O_5. Ethyl ether and THF were dried ($MgSO_4$), refluxed with Na and benzophenone until a blue color formed, and distilled. DMF was vacuum distilled from CaO. Diisopropylamine was dried over KOH pellets and then distilled from CaO. Anhydrous glycerine was obtained by heating Baker anhydrous glycerine under a stream of dry N_2 for 24 h. Precoated silica gel on polyester TLC plates were obtained from Aldrich Chemical Co., Inc. Milwaukee, WI. Merck silica gel Grade 60, 100–200 mesh, and activated Al_2O_3 (ca. 150 mesh) were used for gravity chromatography columns, and Merck silica gel Grade 60, 230–450 mesh, was used for flash chromatography columns.

Spectral data were recorded on the following instruments: ^1H NMR, Varian CFT-20 (80 MgHz), Varian VXR-300, or Brucker WM-500 cryospec spectrometer with Me_4Si as internal standard; ^{13}C NMR, Varian VXR-300 with $CDCl_3$ solvent as the standard; UV–vis, Hewlett-Packard 8450-A spectrophotometer (0.1 or 1.0 cm quartz cells); mass spectra, Hewlett-Packard 5985 GS/MS system with a 30 m (DB-5) fused silica capillary column with perfluorokerosene as the standard. The synthesis of cyclopentanone was carried out several times with unlabeled compounds to find reaction conditions which gave satisfactory yields (products characterized by GC/MS and ^1H NMR) prior to the use of ^{13}C-labeled reagents.

[1,2-$^{13}C_2$]Ethanenitrile. The procedure of Anthoni and Nielsen[8] was used except anhydrous glycerine was replaced by DMF as the solvent. From 2.0 g (31 mmol) of 99% [^{13}C]KCN[9] and 5.0 g (35 mmol) of 99% [^{13}C]CH_3I[9] was obtained 1.04 g (82.5%) of dilabeled enthanenitrile: ^{13}C NMR ($CDCl_3$) δ 116.21 (d, J = 57.96 Hz, CN), 210 (d, J = 57.74 Hz, CH_3), and −23.15 (trace of $^{13}CH_3I$); ^1H NMR ($CDCl_3$) δ 2.0 (dd, J = 135.75 and 9.86 Hz).

[1,2-$^{13}C_2$]-5-Chloropentanenitrile. A solution of 0.28 mL (1.845 g, 18.3 mmol) of freshly distilled diisopropylamine, 7.28 mL (18.3 mmol) of 2.5 M butyllithium in hexanes, and 3.06 mL (3.118 g, 17.4 mmol) of hexamethylphosphoramide in 20 mL of dry diethyl ether was stirred at 0 °C for 30 min. The solution was then added dropwise (syringe) with stirring to a solution of

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(6) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, 4899–4907. Davidson, W. C. *Comp. J.* **1968**, *10*, 406. Fletcher, R.; Powell, M. J. D. *Comp. J.* **1963**, *6*, 163.
(7) Scott, L. T.; Kirms, M. S.; Berg, A.; Hansen, P. E. *Tetrahedron Lett.* **1982**, *23*, 1859. These authors did not report the percent of isotopic enrichment in the product.
(8) Antoni, U.; Nielsen, R. H. *J. Labelled Compd. Radiopharm.* **1984**, *21*(4), 375–80.
(9) ICN - Cambridge Isotopes, Cambridge, MA 02142.

0.7134 g (17.4mmol) of the above ethanenitrile and 1.61 mL (2.83 g, 18 mmol) of 1-bromo-3-chloropropane in 48 mL of dry ether at −79 °C (dry ice–acetone), and the mixture was stirred for 2 h. The solution was slowly (1 h) brought to room temperature, and 20 mL of water was then added. The separated ether layer was washed successively with 1 M hydrochloric acid (three times), saturated $NaHCO_3$, and concentrated NaCl solution. Removal of the solvent from the dried ($MgSO_4$) ethereal solution gave 1.233 g of pale-yellow residue. Chromatography (15 × 2.5 cm silica gel column; elution with 10% CH_2Cl_2 in hexane) afforded 0.253 g (32%) of product which gave a single peak on GC analysis: ^{13}C NMR ($CDCl_3$) δ 16.69 (d, J = 56.2 Hz, C-2), 119.06 (d, J = 55.9 Hz, CN); ^1H NMR ($CDCl_3$) δ 1.85 (m, 2, 3-CH_2), 1.92 (m, 2, 4-CH_2) 2.41 (4 t, 2,2-CH_2, J = 134.9 Hz (to ^{13}C-2), J = 9.78 Hz (to ^{13}CN), $J_{2,3}$ = 6.5 Hz), 3.59 (2 t, 2, 5-CH_2, J = 2.2 Hz (to ^{13}C-2), $J_{4,5}$ = 5.97 Hz).

[1,2-$^{13}C_2$]-5-Iodopentanenitrile. A mixture of 0.2534 g (2.17 mmol) of the above 5-chloropentanenitrile, 0.75 g (5 mmol) of NaI, and 10 mL of acetone was refluxed for 24 h. Diethyl ether (20 mL) was added to the cooled mixture, and the whole was washed with two 10-mL portions of H_2O, 0.1 M Na_2SO_3, and concentrated NaCl solution. Removal of the solvent from the dried ($MgSO_4$) ethereal solution afforded 0.375 g (79%) of the iodo product as a pale yellow oil:[10] ^{13}C NMR ($CDCl_3$) δ 16.33 (d, J = 56.0 Hz, C-2), 119.01 (d, J = 56.2 Hz, CN); ^1H NMR ($CDCl_3$) δ 1.79 (m, 2, 4-CH_2), 1.97 (m, 2, 3-CH_2), 2.40 (4 t, 2, 2-CH_2, J = 134.7 Hz (to ^{13}C-2), J = 9.66 Hz (to ^{13}CN), $J_{2,3}$ = 6.5 Hz), 3.22 (2 t, 2, 5-CH_2, J = 2.2 Hz (to ^{13}C-2), $J_{4,5}$ = 6.5 Hz).

[1,2-$^{13}C_2$]Cyclopentanone. To a solution of 0.3575 g (1.7 mmol) of the above 5-iodopentanenitrile in 60 mL of dry diethyl ether cooled to −79 °C (dry ice–acetone) under Ar was added dropwise (syringe) 1.1 mL (1.7 equiv) of 1.7 M *tert*-butyllithium in pentane. The solution was stirred for 1 h and then allowed to come to room temperature. After 2 h, the solution was washed with 30 mL of saturated $(NH_4)_2SO_4$, 10 mL of aqueous Na_2SO_3, and twice with concentrated NaCl solution. Removal of the solvent from the dried ($MgSO_4$), filtered ether layer by distillation through a 7.6-cm Vigreux column left 0.466 g of crude product. Chromatography on a 20 × 2.5 cm silica gel column (elution with 120 mL of pentane then 10% CH_2Cl_2 in pentane) followed by solvent removal as before gave 0.117 g (1.36 mmol, 80%) of labeled cyclopentanone: R_f = 0.25 on a silica gel plate developed with CH_2Cl_2 and visualized with an anisaldehyde dip; ^{13}C NMR ($CDCl_3$) δ 38.26 (d, $J_{1,2}$ = 37.2 Hz, C-2), 220.12 (d, $J_{2,1}$ = 37.0 Hz, C-2); mass spectrum, m/e (relative intensity) 86 (M^+, 25), 57 (M^+ −29, 93), 56 (M^+ − 30, 55), 43 (M^+ − 43, 64), 41 (M^+ − 45, 100).

[2a,11-$^{13}C_2$]Azupyrene. This compound was synthesized as previously described[2] using the above labeled cyclopentanone diluted (by weight) to 18% ^{13}C enrichment. A second dilution to 1.94% ^{13}C was made at the trimethyleneazulene stage. The ^{13}C NMR spectra of the labeled *N*-cyclopentylidenedimethylammonium fluoroborate, dimethyl[5-(dimethylamino)-1,2-trimethylenepentadien-2,4-ylidene]ammonium fluoroborate, and 4,5-trimethyleneazulene intermediates were recorded.[1] The ^{13}C NMR spectrum ($CDCl_3$) of the azupyrene product exhibited δ 133.60 (d, J = 50.3 Hz, C-2a), 140.82 (d, J = 50.8 Hz, C-11). The ^{13}C enrichment at C-2a was 1.96% and that at C-11 was 1.87% (average = 1.915%) based on the relative intensities of the doublets and the corresponding peaks from the natural abundance azupyrene.

Thermal Isomerization of [2a,11-^{13}C]Azupyrene. In a 13-cm quartz tube (9 mm o.d., 7 mm i.d.) with a constriction 3.8 cm from the closed end and which had been washed with nitric acid, H_2O, and acetone and then dried at 120 °C was placed a solution of 8.5 mg (0.042 mmol) of natural or 1.915% $^{13}C_2$ enriched azupyrene in acetone. After the solvent had evaporated, the tube was swept with Ar for 1 h, evacuated to 0.5 Torr pressure, and sealed (H_2 flame). This was heated (electric furnace lined with a quartz tube) at 450–460 °C (calibrated thermocouple) for 5–6 h. The cooled tube and contents were crushed (mortar and pestle) and extracted five times with CH_2Cl_2. Removal of the solvent from the combined extracts left 3.9 mg (45%) of pyrene. A total of five runs were performed, three with unlabeled and two with labeled azupyrene. The ^{13}C NMR spectra of natural ^{13}C abundance pyrene and of the enriched pyrene were taken and used to determine the positions of ^{13}C enrichment in the labeled material. The ^{13}C peak assignments for natural pyrene were ($CDCl_3$) δ 130.99 (s, C-3a,-5a,-7a,-10a), 127.44 (s, C-4,-5,-9,-10), 125.70 (s, C-2,-7), 124.81 (s, C-1,-3,-6,-8), 124.54 (s, C-11,-12) (confirmed by the APT spectrum). The spectrum of the ^{13}C enriched product showed corresponding peaks at δ 130.97 (s and d), 127.21 (s), 125.68 (s), 124.81 (s), and 124.51 (s and d) with doublets due to coupled ^{13}C atoms at adjacent quaternary positions.

Measurement of the peak intensities (natural abundance spectrum) at delay times of 4, 8, 15, 30, 60, and 120 s and normalization of these relative to the intensity of the peak at δ 124.81 showed that there was complete relaxation with respect to the peak at δ 124.51 at 30 s or longer, and with respect to the peak at δ 130.97 at 60 s or longer. The small amount of pyrene obtained (<8 mg) from the isomerization runs made the acquisition time for a delay longer than 30 s prohibitive, so this time was used for the spectrum of the enriched (isomerization product) pyrene. The peak intensities used as standards were obtained by averaging the normalized intensities for the three natural abundance samples. For the spectrum of the ^{13}C enriched product, one peak of the doublet at δ 124.51 was covered by the large singlet.

Normalization of the peaks in the ^{13}C-enriched spectrum successively with respect to each of the other peaks using the relationship $(I/I_{ref})100$ showed that all positions were partially enriched (ratio for enriched material greater than corresponding ratio for natural abundance material) and that the peak at δ 124.81 as a reference gave the most consistent comparisons. The per unit enrichment relative to natural abundance at the quaternary carbons was determined from the doublet at δ 130.97 to be 1.165 (average of two runs).[11] Thus it appeared that 0.76% of the enrichment in the labeled azupyrene had been distributed evenly among the other pyrene carbons.

Thermal Automerization of [3a,11-$^{13}C_2$]Pyrene. A sample of the ^{13}C-enriched pyrene obtained from the isomerization of [2a,11-$^{13}C_2$]azupyrene was heated as described for the latter process for 5.5 h. The ^{13}C NMR spectrum ($CDCl_3$) of the recovered pyrene (no azupyrene was detected) showed peak intensities (normalized to 100 for δ 127.21) of 55.7 (δ 130.97), 100 (127.21), 46.6 (125.68), 103.6 (124.81), and 24 (124.51) as compared to 51.4, 100, 47.2, 110.8, and 25.2 for the corresponding peaks for natural abundance pyrene.

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(11) The intensity of the visible peak of the other doublet at δ 124.51 was less reliable because of the overlap with the broad singlet.