(14) All four possible geometrical isomers, 2Z,6Z, 2E,6Z, 2Z,6E, and 2E,6E, are separable by GLC with an order of elution as given in this listing.[8c]
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Synthesis of 7-Fluorobenz[*a*]anthracene[1]

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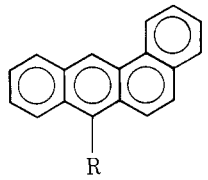
The desirability of testing 7-fluorobenz[*a*]anthracene (**1**) for carcinogenic activity has increased as more was learned about the carcinogenic activity of substituted benz[*a*]anthracenes. The fact that 7-methylbenz[*a*]anthracene (**2**) is the most potent carcinogen of the monomethyl benz[*a*]anthracenes[3] has been explained by two essentially different hypotheses.[4] In one, a metabolic change leading to cancer occurs in the 7-methyl group and in the other, the 7-methyl group confers activity because it blocks a detoxification metabolism which starts at the 7 position.[3] The testing of 7-fluorobenz[*a*]anthracene was deemed important because the 7-fluoro atom could block a detoxification mechanism but would not allow for a carcinogenic metabolism at the fluorine atom.

Attempts at synthesis of **1** have been made[5-7] but insufficient **1** had been made for adequate testing at the time we started the work reported. Our successful route involves the diazotization of 7-aminobenz[*a*]anthracene (**3**) by dry gaseous nitric oxide in dry ether followed by nitrogen dioxide and treatment with HBF_4 (or HPF_6) to give a diazomium salt, **4**, which could be dried and pyrolyzed to yield pure **1** in good yield.[8] This route is essentially that used to convert 9-aminoanthracene into 9-fluoroanthracene.[9] All other diazotization procedures attempted failed to give products which would yield any **1** on pyrolysis. That **1** had the fluorine in the 7 position was supported by the facts that oxidation afforded 7,12-benz[*a*]anthraquinone in high yield and the NMR spectrum had a 1 proton singlet at δ 8.84, characteristic of H_{12} in 7-substituted benz[*a*]anthracenes.[10]



1, R = F
2, R = CH_3
3, R = NH_2
4, R = $N_2^+BF_4^-$
5, R = NO_2
6, R = H

7-Nitrobenz[*a*]anthracene (**50**) was prepared by an improved procedure which affords **5** in 55% yield from benz[*a*]anthracene (**6**). The starting **6** was prepared by condensation of phthalaldehydic acid with naphthalene to yield 3-(1-naphthyl)phthalide[11] which was reduced to 2-(1-naphthylmethyl)benzoic acid[12] followed by ring closure, reduction of benzanthrone, and dehydration to yield **6** in 76% overall yield. Compound **1** is being tested for carcinogenic activity.

Experimental Section[13]

2-(1-Naphthylmethyl)benzoic Acid. 3-(1-Naphthyl)phthalide[11] (76 g, 0.29 mol) was combined with 400 g of Zn dust (activated by washing with dilute HCl) and 2 L of 90% formic acid. After refluxing the vigorously stirred mixture for 72 h the liquid portion was decanted into 1.5 L of ice water. The resulting white solid was collected and the mother liquor as well as the zinc residues were washed with 1 L of ether–benzene. After dissolving the product in ether–benzene, usual treatment of the combined organic phases gave 65.5 g (85%) of white solid, mp 144.0–146.0 °C (lit.[12] mp 148–148.5 °C), suitable for use in the next step.

Benz[*a*]anthracene (6) 2-(1-Naphthylmethyl)benzoic acid (20 g, 76.5 mmol) was added to 250 mL of anhydrous HF. After 20 min the red solution was poured onto 1 kg of ice. The pale yellow solid was collected, washed with water, and added to a flask containing 75 g of Zn dust (activated with $CuSO_4$), 800 mL of 2 N NaOH, and 200 mL of toluene.[14] After refluxing the solution for 18 h, an additional 25-g portion of activated Zn was added. After a total reflux time of 48 h, the reaction mixture was cooled to 80 °C and 200 mL of benzene added. The liquid portion was decanted and the solids washed with an additional 200 mL of benzene. The organic phase was separated and treated as usual to give 16.63 g (94%) of colorless **6**, mp 155.0–156.5 °C. Recrystallization from ethanol–benzene gave 15.59 g (89.5%), mp 157.0–158.0 °C (lit.[15] mp 160.5–161 °C).

7-Nitrobenz[*a*]anthracene (5). A solution of 10 g (44 mmol) of **6** and 600 mL of CH_2Cl_2 was cooled to −15 °C and 3.2 g of 90% HNO_3 (46 mmol) was added over 15 min. The temperature was raised to 0 °C and 2.5 g of additional HNO_3 was added over 1.5 h. Addition of 100 mL of water followed by the usual workup gave 12 g of orange solid. Recrystallization from ethanol–benzene (4:1) gave 6.61 g (55%) of yellow **5**, mp 159.0–161.0 °C (lit.[5] mp 163–164 °C), suitable for reduction to **3** as described.[16]

7-Diazoniumbenz[*a*]anthracene Tetrafluoroborate (4). A yellow solution of 1.0 g (4.28 mmol) of **3**[16] in 150 mL of anhydrous ether was flushed with N_2 and cooled in an ice bath. Nitric oxide (supplied by Matheson and passed through a concentrated H_2SO_4 scrubber) was bubbled slowly through the solution for 1 h to produce a cinnamon-colored, nonhomogeneous mixture. Dry air was then combined with the NO flow to generate NO_2, which was passed through the mixture for 1 h. During this period an orange precipitate formed. The addition of 4 mL of 48% HBF_4 caused no observable color change. After 0.5 h the bright orange solid was collected, washed with ether, and dried in a vacuum desiccator to give 1.22 g (90%) of **4**, mp 118.0–120.0 °C dec. A similar result was obtained using HPF_6 instead of HBF_4 but the mp was not sharp and not reproducible.

7-Fluorobenz[*a*]anthracene (1). A mixture of 0.5 g (1.57 mmol) of **4** and 0.5 g of powdered dry KF was added over 0.5 h to 50 mL of refluxing xylenes. The resulting dark solution was filtered and evaporated to dryness. The residue was dry column chromatographed[17] on 90 g of silica gel[18] in a 0.75 in. × 20 in. Nylon column using hexane as the eluant. Under these conditions the product band moves most rapidly (R_f 0.5) and separates from impurities (short wave UV light used to visualize bands). The band was cut out and extracted with ether to yield 350 mg (91%) of pure **1**, mp 93.5–94.3 °C. A similar pyrolysis on three times the scale resulted in a 72% yield of pure **1**. Neat pyrolysis on a 3 mmol scale afforded only 60% of pure **1**. The following spectral data were obtained: mass spectra; parent ion *m/e* 246 (rel intensity 100); NMR ($CDCl_3$, Me_4Si) δ 8.84 (s), 8.84–8.60 (m, 2 H, H_{12}, and H_1 respectively), 8.35–7.4 (complex multiplet, 9, H, all remaining protons).[10] Repeated recrystallization from ethanol to obtain an analytical sample did not raise the mp over 93.8–94.3 °C. Anal. Calcd for $C_{18}H_{11}F$: C, 87.8; H, 4.5; F, 7.7. Found: C, 87.8; H, 4.6; F, 7.6.

Benz[*a*]anthracene-7,12-dione. A solution of 100 mg of **1**, 7 mL of glacial acetic acid, and 130 mg of sodium dichromate was refluxed for 0.5 h. The resulting green solution was added to 10 mL of water. The yellow solid was collected, washed with water, and oven dried to yield 100 mg of quinone, mp 166.0–168.5 °C. Recrystallization from benzene–ethanol afforded yellow quinone mp and mmp with authentic quinone (supplied by Eastman) 167.0–168.5 °C (lit.[19] mp 168 °C). Mass spectrum showed a parent ion of *m/e* 258.

Registry No.—**1**, 23683-26-3; **3**, 2381-18-2; **4**, 69238-66-0; **5**, 20268-51-3; **6**, 56-55-3; benz[*a*]anthracene-7,12-dione, 2498-66-0; 2-(1-naphthylmethyl)benzoic acid, 69238-67-1; 3-(1-naphthyl)-phthalide, 56282-14-5.

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Simple Stereospecific Synthesis of *endo*-Norbornyl Chloride

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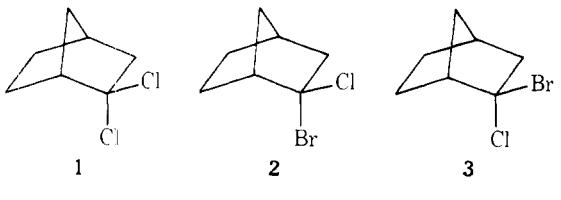
exo-Norbornyl chloride can be prepared easily in very high isomeric purity by the addition of hydrogen chloride to norbornene.[2] However, difficulties have been encountered in preparing *endo*-norbornyl chloride free of the epimeric exo compound.

Roberts and his co-workers[3] synthesized *endo*-norbornyl chloride by the hydrogenation over PtO_2 of 5-chloro-2-norbornene prepared by the Diels–Alder condensation of cyclopentadiene with vinyl chloride. However, solvolytic studies revealed that it was contaminated with the more reactive *exo*-chloride. Indeed, the product proved to be a mixture of 87% *endo*- and 13% *exo*-chloride. Repeated solvolysis of the above mixture ultimately yielded *endo*-chloride of 95% purity.[4]

In the literature several other procedures for preparing *endo*-norbornyl chloride have been reported. However, none of these procedures yields the isomerically pure compound. Free-radical chlorination of norbornane gives predominantly the 2-chlorides, with exo/endo product ratios depending upon the precise nature of the chlorine donor.[5] Thus, molecular chlorine gives about 70% exo and 20–25% endo. The more selective chlorinating agents, SO_2Cl_2, CCl_4, and PCl_5, give approximately 95% exo.

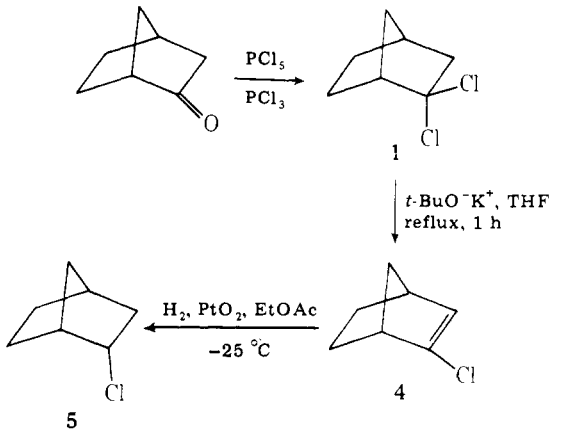
The reaction of *exo*-norbornanol with triphenylphosphine and carbon tetrachloride gives the 2-norbornyl chlorides in a molar ratio of 3.8–3.5:1.0 exo/endo.[6]

The controlled potential electrochemical reduction[7] at a mercury cathode of 2,2-dichloronorbornane (**1**), *exo*-chloro-*endo*-bromonorbornane (**2**), or *exo*-bromo-*endo*-chloronorbornane (**3**) gave similar mixtures of *endo*-norbornyl chloride (36–80%) and nortricyclane (64–20%).



1 2 3

Scheme I



Cristol and his co-workers[8] established that the photosensitized irradiation of purified *endo*-chloronorbornene with a variety of sensitizers and solvents led to the saturation of the double bond to form *endo*-norbornyl chloride in yields of approximately 10%.

Brown and De Lue[9] observed that the reaction of nitrogen trichloride with tri-*exo*-norbornylborane gave a mixture of the two epimeric chlorides, 77% *exo*- and 23% *endo*-chloride.

For our solvolytic studies we desired to utilize isomerically pure *endo*-norbornyl chloride. Since none of the published procedures would give us the pure endo compound, we undertook to prepare *endo*-norbornyl chloride (**5**) by a stereospecific route, as illustrated in Scheme I. 2,2-Dichloronorbornane (**1**) was prepared following the literature procedure[10] and converted into 2-chloronorbornene (**4**) by a modified procedure which reduced the reaction time from 40 to 1 h.[11] Next, 2-chloronorbornene was hydrogenated in ethyl acetate using PtO_2 as catalyst in a Brown hydrogenator.[12] When the hydrogenation was carried out at 25 °C, considerable reductive dehalogenation was observed. In order to minimize reductive dehalogenation, the low-temperature procedure developed by C. A. Brown[13] was utilized. He had observed that the rates of hydrogenation of olefins were remarkably insensitive to decreases in the temperature of hydrogenation. Even more important, such hydrogenations at lower temperatures show considerable improvements in the selectivity of the reaction. Indeed, as the temperature of hydrogenation of 2-chloronorbornene was lowered, less and less reductive dehalogenation was observed. GC analysis of the product hydrogenated at −25 °C revealed a yield of *endo*-norbornyl chloride of 90%. There was readily isolated an 82% yield of the pure product, mp 44–45 °C. These results are summarized in Table I.

The product, *endo*-norbornyl chloride, was examined carefully, both by ^{13}C and ^{1}H NMR spectroscopy, and was evidently free of the epimer.

Table I. Hydrogenation of 2-Chloronorbornene. Effect of Temperature on the Selectivity of Hydrogenation

		% product[c]	
temp,[a] °C	$T_{100\%}$, min[b]	*endo*-norbornyl chloride[e]	norbornane[f]
25	60	62	38
0	100	70	30
−10	135	75	25
−25	200	90 (82)[d]	10

[a] Temperatures were held to ±1 °C. [b] Time for complete reduction. [c] GC yield. [d] Isolated yield. [e] Registry no., 2999-06-6. [f] Registry no., 279-23-2.

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