The Synthesis of Specifically Deuterated Anthracenes

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Synthetic methods for preparation of anthracene-1,2,3,4-d_4, 1,4,5,8-d_4, 2,3,6,7-d_4, 2,3-d_2, 1,4-d_2, and 9,10-d_2 are described.

On décrit des méthodes spécifiques de synthèse pour la préparation de l'anthracène-1,2,3,4-d_4, -1,4,5,8-d_4, 2,3,6,7-d_4, -2,3-d_2, -1,4-d_2 et 9,10-d_2. [Traduit par le journal]

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Recently, there has been considerable theoretical interest in the mechanism of radiationless transitions in aromatic molecules and, in particular, the effect of various substituent groups on the rate of these transitions (1). In this regard, it has been popular to determine experimentally the triplet lifetimes of specifically deuterated compounds and to correlate the results with theoretically calculated values. In particular, we wished to carry out such a study utilizing the deuterated derivatives of anthracene listed in Table 1.

Of the derivatives listed, only anthracene-9,10-d_2 (**1**) has been mentioned previously in the literature. It was first synthesized by treating anthracene with D_2SO_4. However, the procedure also gave mono and other polydeuterated products from which **1** was inseparable (2). **1** can be synthesized specifically by hydrolyzing the corresponding dimagnesium derivative with D_2O (99.8%) but preparation of the Grignard is difficult (3, 4). The most successful synthetic method involves preparation of the dilithio derivative followed by hydrolysis with D_2O. Using this method, Petukhov *et al.* originally reported synthesizing **1** in 72% isotopic purity (5). However, Pawliczek and Günther reported isotopic purities of greater than 97% using essentially the same method (6).

Two main synthetic routes are possible for the remaining derivatives in Table 1. Either the deuterium can be introduced after the carbon skeleton is constructed or the molecule can be prepared from suitably deuterated precursors. In the former method metalation and D_2O hydrolysis of the aromatic halides has been one of the more popular methods of approach. However, problems are often encountered in preparing the organometallic derivatives and the isotopic purity of the product is variable (3). The best published method for the preparation of perdeuterated anthracene is that of Dinh-Nguyên and Stenhagen (7) using D_2O_2 and a catalyst. The perdeutero compound can also be prepared by base or acid catalyzed deuterium exchange and the latter method is also suitable for specific deuteration if the rates of exchange are sufficiently position dependent. (8, 9, 2). Synthesis of the deuterated aromatics from deuterated precursors can be successful if a high yield procedure, which utilizes relatively simple starting materials, is available.

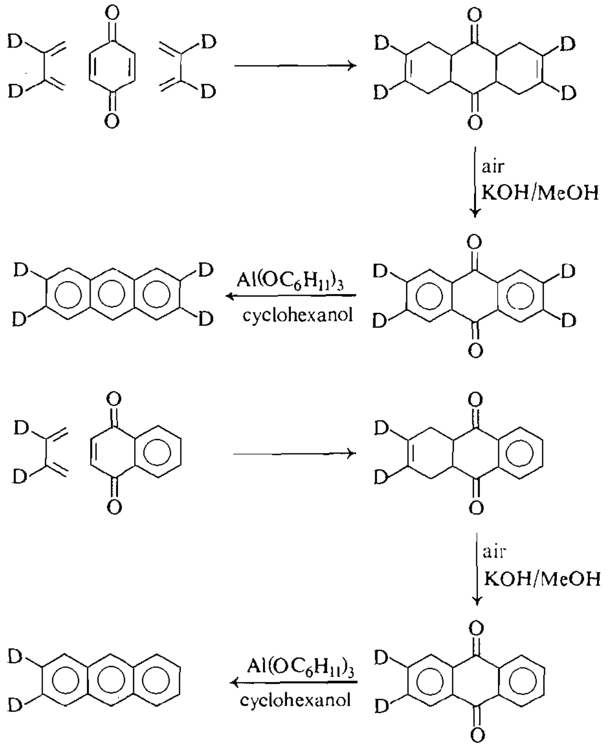
TABLE 1. Isotopic composition of deuterated anthracenes synthesized

Anthracene	Purity (%)*		
9,10-d_2 (**1**)	7.0 d_1†	85.0 d_2	7.0 d_3
	11.6 d_1‡	88.0 d_2	
2,3-d_2 (**2**)	4.2 d_0	9.5 d_1	86.0 d_2
1,4-d_2 (**3**)	5.1 d_0	3.8 d_1	91.2 d_2
1,4,5,8-d_4 (**4**)	1.1 d_2	3.6 d_3	95.3 d_4
2,3,6,7-d_4 (**5**)	7.6 d_2	17.0 d_3	74.0 d_4
1,2,3,4-d_4 (**6**)	3.7 d_0	7.0 d_3	88.0 d_4

*Mol. % isotopic composition. Values are precise to only ±2%.
†Method *b*; see Experimental.
‡Method *a*; see Experimental.

Results and Discussion

Anthracene-9,10-d_2 was synthesized both by the method of Petukhov *et al.* (5) and by acid-catalyzed deuterium–hydrogen exchange. The former method involved treating 9,10-dibromoanthracene with *n*-butyl lithium in benzene to prepare the 9,10-dilithioanthracene. This was subsequently hydrolyzed with D_2O yielding the dideutero derivative. This reaction was carried out several times and the isotopic purity (mol % dideutero) was never higher than 90% (the remaining 10% being monodeutero). As an alternative procedure we considered a mild



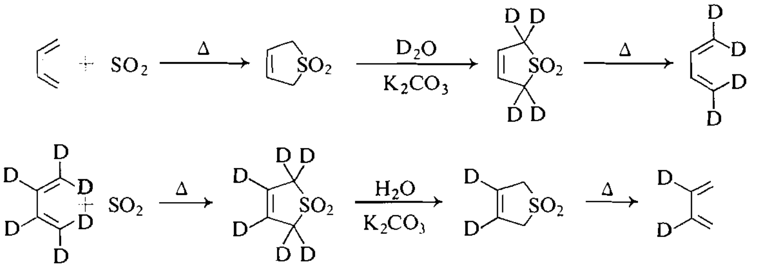
SCHEME 1

acid-catalyzed exchange reaction as the 9,10 positions in anthracene should exchange more rapidly. Since it had already been reported that D_2SO_4 gave a mixture of both mono and polydeuterated material a weaker acid was sought. *p*-Toluenesulfonic acid-*d* was chosen both because of its higher pK_a and its solubility in organic solvents. The acid was prepared *in situ* by adding D_2O to a mixture of anthracene and *p*-toluenesulfonyl chloride in benzene. The exchange occurred rapidly in refluxing benzene after an induction period of up to 48 h. This led us to believe that the hydrolysis of the acid chloride was rate limiting and probably autocatalytic. Although the method used was satisfactory it would probably be more expedient to hydrolyze the sulfonylchloride in a separate step. The product was isolated by stirring the mixture with saturated aqueous bicarbonate overnight and extracting with benzene. The isotopic composition was 85% d_2, 7% d_3, and 7% d_1 (mol %).

After considering the various possibilities for synthesis of the remaining anthracene derivatives we concluded that a scheme based on the Diels–Alder adducts of deuterated butadienes with *p*-benzoquinone or 1,4-naphthoquinone was best. Two representative examples are illustrated in Scheme 1. The basic procedure had been successfully carried out on the nondeuterated analogs by Alder and Stein (10) and by Diels and Alder (11).

In order to utilize the diene synthesis it was necessary to prepare specifically deuterated butadienes. These were prepared using known literature procedures or modifications of these procedures. Perdeutero-1,3-butadiene was synthesized from perchlorobutadiene using zinc and D_2O as described by Craig and Fowler (12). The yields varied from run to run but were generally around 50%. The syntheses of 1,3-butadiene-1,1,4,4-d_4 and -2,3-d_2 are outlined in Scheme 2.

The 3-sulfolenes were prepared from the corresponding butadienes and SO_2 by the method of Grummitt *et al.* (13) and the base-catalyzed exchange accomplished as described by Cope *et al.* (14). The deuterated butadienes were subsequently recovered by pyrolyzing the sulfolenes at 130–160 °C under a slow stream of nitrogen. The Diels–Alder adducts of the



SCHEME 2

deuterated butadienes and *p*-benzoquinone (or 1,4-naphthoquinone) were formed by heating the quinone in an excess of the butadiene at 125 °C for 24 h in a sealed evacuated tube. The yields were quantitative in most cases.

The method of Alder and Stein was also used for the oxidation of the octahydroanthraquinones to the quinones (10). However, it was noted that this base-catalyzed oxidation (air and ethanolic KOH) led to some isotope exchange, especially in the 2,3,6,7-d_4 derivative. This was probably due to a base-catalyzed exchange in the partially oxidized material although it was surprising that it was more severe in the 2,3,6,7-d_4 derivative than in the 1,4,5,8-d_4 derivative. Presumably an alternate oxidation method would eliminate this problem but no other method was attempted in this study.

The reduction of the anthraquinone was achieved using aluminum tricyclohexyloxide in cyclohexanol (15). Although the yields of purified anthracene were very low, this generally reflects extensive purification by chromatography and recrystallization rather than inefficiency in the reduction step.

Table 1 lists the anthracenes synthesized and their isotopic purities as determined by low voltage mass spectrometry (8 eV).

Experimental

Mass spectra were recorded on a Finnigan 1015 mass spectrometer at an ionization energy of 8 eV. Mass ratios were calculated from peak heights and are precise only to ±2%. N.m.r. spectra were recorded on a Varian A56-60 spectrometer and chemical shifts are recorded in p.p.m. downfield from tetramethylsilane. $CDCl_3$ was the solvent used unless otherwise specified.

Anthracene-9,10-d_2 (1)

(*a*) Butyl lithium (0.01 mol in 3 ml benzene) was added to a solution of 9,10-dibromoanthracene (1.0 g, 0.003 mol) in benzene (35 ml) under nitrogen.

After refluxing 40 min and cooling, D_2O (2 ml) was added and the solution stirred 5 min. The benzene was then washed three times with water, dried ($MgSO_4$) and evaporated to leave a yellow crystalline residue. Ten recrystallizations from chloroform followed by treatment with Norit in chloroform gave 50 mg of blue fluorescent plates.

Mass spectrum: *m/e* (relative intensity) 178(4.9), 180(32), 181(5.0).

(*b*) Anthracene (0.78 g, Baker sensitizer grade) was refluxed in benzene (100 ml) containing *p*-toluene sulfonyl chloride (10 g) and D_2O (2 ml). Progress of the exchange reaction was followed by mass spectrometry. After 30 h the reaction mixture was diluted with benzene (100 ml) and extracted with aqueous sodium bicarbonate (5%). The benzene fraction was evaporated to dryness and the residue heated on a steam bath for 15 h with 100 ml of saturated aqueous sodium bicarbonate. Extraction with $CHCl_3$, drying ($MgSO_4$), and evaporation yielded the crude anthracene-9,10-d_2. This was recrystallized from $CHCl_3$, with treatment with charcoal, to yield blue fluorescent crystals.

Mass spectrum: *m/e* (relative intensity) 179(3.5), 180(42), 181(10.1). N.m.r.: δ 7.46 (m, 4H), 8.03 (m, 4H).

1,3-Butadiene-d_6

The method of Craig and Fowler (12) was used with slight modification. Zinc dust (98 g) and anhydrous dioxane (114 g) were placed in a 500 ml round-bottomed flask fitted with a nitrogen inlet, dropping funnel, condenser, and stirrer. The condenser was connected to a Dry Ice trap. After flushing with nitrogen, NaI (0.8 g), anhydrous CuCl (4.8 g) and D_2O (26.4 g) were added. The mixture was refluxed with stirring and hexachlorobutadiene (52 g) was added over 1 h. The yield of crude product was 7.25 ml (44%).

Mass spectrum: *m/e* (relative intensity) 59(8.7), 60(59.9), 61(3.1).

3-Sulfolene-d_6

The method of Grummitt *et al.* (13) was used with slight modification. 1,3-Butadiene-d_6 (12 ml), sulfur dioxide (13.5 ml), and hydroquinone (0.10 g) were sealed in a thick-walled glass tube after evacuation at −79 °C to 10^{-2} mm Hg. The mixture was heated at 100 °C for 12 h. The crude reaction mixture was dissolved in water and filtered. Evaporation of the water *in vacuo* and recrystallization from methanol gave 15.8 g of yellowish-white crystals (84%).

Mass spectrum: *m/e* (relative intensity) 59(11.0), 60(89.2), 61(4.2).

3-Sulfolene-2,2,5,5-d_4

The method of Cope *et al.* (14) was used with slight modification. 3-Sulfolene (10.0 g), potassium carbonate

(0.11 g), D_2O (10 g), and anhydrous dioxane (10 ml) were stirred at room temperature for 48 h. The solvents were removed *in vacuo* at room temperature, fresh D_2O and dioxane added, and the solution again stirred 48 h. This procedure was repeated seven times and the residue was dried at room temperature under high vacuum. The product was used in the next step without purification.

Mass spectrum: *m/e* (relative intensity) 57(3.9), 58(31.9), 59(1.8).

1,3-Butadiene-1,1,4,4-d_4

The dried sulfolene-d_4 sample from above was placed in a round-bottomed flask fitted with a nitrogen inlet and connected in series through two gas absorption traps (each containing 25 ml of 20% aqueous NaOH) and a drying tube (Drierite) to a Dry Ice trap. Nitrogen gas was slowly passed through the system and the sample heated to 130–160 °C for 1.5 h. Five milliliters (79%) of butadiene was collected.

3-Sulfolene-3,4-d_2

The perdeutero-3-sulfolene (7.12 g) was treated with H_2O in a manner analogous to the treatment of perhydro-3-sulfolene with D_2O (described above) yielding 6.0 g of the 3-sulfolene-3,4-d_2 (87%) (some insoluble material formed during the exchange and was filtered off).

Mass spectrum: *m/e* (relative intensity) 55(2.8), 56(70.0), 57(3.9).

1,3-Butadiene-2,3-d_2

The 3-sulfolene-3,4-d_2 was pyrolyzed as described previously (for 3-sulfolene-2,2,5,5-d_4) to yield 2.2 ml of 1,3-butadiene-2,3-d_2 (59%).

1,3-Butadiene-1,1,4,4-d_4-p-benzoquinone Adduct

The procedure was generally similar to that of Alder and Stein (10). 1,3-Butadiene-1,1,4,4-d_4 (2.0 g) was distilled into a thick-walled glass tube containing *p*-benzoquinone (1.0 g) and benzene (2 ml). The tube was degassed by three freeze–thaw cycles with evacuation to 10^{-2} mm Hg, then sealed and heated at 120 °C for 24 h. After cooling the product separated as white crystals and, after evaporation of the benzene, was used without further purification. Yield was 2.0 g (100%).

Anthraquinone-1,4,5,8-d_4

The anthraquinone was prepared from the octahydroanthraquinone using the method of Alder and Stein (10). The adduct from above (2.0 g) was refluxed in 5% ethanolic KOH (50 ml) with a stream of air passing through the mixture for 1 h. The mixture was diluted with water, neutralized with 1 *N* HCl, and the quinone extracted with $CHCl_3$. The combined extracts were dried ($MgSO_4$) and evaporated to dryness to yield 1.89 g (98%) which was used without further purification.

Anthracene-1,4,5,8-d_4 (4)

Anthraquinone-1,4,5,8-d_4 from above (1.0 g), aluminum tricyclohexyloxide solution (10 ml, see preparation below), and cyclohexanol (5 ml) were refluxed 48 h. The solution was poured into water (50 ml), benzene added (50 ml), and the mixture filtered, washing the residue well with hot benzene. The benzene and water were separated and the water extracted with benzene. The benzene solutions and extracts were combined and evaporated *in vacuo*. The residual cyclohexanol was removed as an azeotrope with water and benzene. The anthracene was chromatographed on alumina (Woelm, GrI; eluant benzene) and recrystallized five times from chloroform. Yield of blue fluorescent crystals, 0.173 g (21%).

Mass spectrum: *m/e* (relative intensity) 181(2.9), 182(91.8), 183(15.3).

N.m.r.: δ 7.46 (s, 2H), 8.42 (s, 4H).

Aluminum Tricyclohexyloxide Solution

Aluminum wire (5 g), cyclohexanol (100 ml, distilled from CaO), mercuric chloride (25 mg), and CCl_4 (1 ml) were refluxed overnight. The solution was used without further treatment.

1,3-Butadiene-1,1,4,4-d_4-1,4-naphthoquinone Adduct

1,3-Butadiene-1,1,4,4-d_4 (5 ml), 1,4-naphthoquinone (11.0 g), and ethanol (5 ml) were heated in an evacuated, sealed heavy-walled glass tube at 100 °C for 3 h. The solvent was removed *in vacuo* and the product used without further purification.

Anthraquinone-1,4-d_2

The crude adduct from above (6.2 g) was oxidized in 5% ethanolic KOH (*ca.* 50 ml) with air as previously described to yield 2.55 g of crude anthraquinone-1,4-d_2.

Anthracene-1,4-d_2 (3)

The crude anthraquinone-1,4-d_2 (2.0 g) was reduced as previously described with aluminum tricyclohexyl oxide (20 ml of prepared solution) to give, after purification, 84.5 mg of anthracene-1,4-d_2 (5%).

Mass spectrum: *m/e* (relative intensity) 178(4.5), 179(3.8), 180(80.0), 181(13.0).

N.m.r.: δ 7.45 (m, 4H), 8.00 (m, 2H), 8.40 (m, 4H).

1,3-Butadiene-2,3-d_2-p-benzoquinone Adduct

1,3-Butadiene-2,3-d_2 (2.2 ml), *p*-benzoquinone (0.65 g), and benzene (2.5 ml) were sealed in an evacuated thick-walled tube and heated to 120 °C for 24 h. The slightly yellow crystalline product (1.17 g) was used without further purification.

Anthraquinone-2,3,6,7-d_4

The adduct from above (1.17 g) was air-oxidized in 5% methanolic KOH (*ca.* 50 ml) as previously described to yield 0.67 (71%) of crude anthraquinone which was not further purified.

Anthracene-2,3,6,7-d_4 (5)

Anthraquinone-2,3,6,7-d_4 (0.64 g) was reduced with aluminum tricyclohexyloxide (12 ml of prepared solution) as previously described to yield 81 mg of purified anthracene-2,3,6,7-d_4 (14.5%).

Mass spectrum: *m/e* (relative intensity) 180(7.4), 181(17.0), 182(72.2), 183(13.8).

N.m.r.: δ 8.01 (s, 2H), 8.44 (s, 2H).

1,3-Butadiene-2,3-d_2-1,4-naphthoquinone Adduct

The adduct was prepared as described above from 1,3-butadiene-2,3-d_2 (0.42 ml) and 1,4-naphthoquinone (1.2 g) in 2 ml ethanol. The crude product (1.56 g, 97%) was used without further purification.

Anthraquinone-2,3-d_2

The adduct from above (1.56 g) was air-oxidized in 5% ethanolic KOH (*ca.* 30 ml) yielding 1.13 g (72%) of the anthraquinone after work-up (see above).

Anthracene-2,3-d_2 (2)

The crude anthraquinone-2,3-d_2 (1.13 g) was reduced with aluminum tricyclohexyloxide (6 ml of prepared solution) in the previously described manner to yield 0.167 g of anthracene-2,3-d_2 (17.2%) after purification.

Mass spectrum: *m/e* (relative intensity) 178(4.0), 179(9.3), 180(8.3), 181(14.1).

N.m.r.: δ 7.46 (m, 2H), 7.98 (m, 4H), 8.43 (s, 2H).

1,3-Butadiene-d_6-1,4-naphthoquinone Adduct

The adduct was prepared, as previously described, from butadiene-d_6 (8 ml) and 1,4-naphthoquinone in 15 ml of ethanol. Work-up yielded 14.2 g (89%) of the crude adduct used without purification.

Anthraquinone-1,2,3,4-d_4

The adduct above (14.2 g) was air-oxidized in 5% ethanolic KOH (*ca.* 100 ml) to yield 13.8 g (100%) of crude anthraquinone-1,2,3,4-d_4.

Anthracene-1,2,3,4-d_4 (6)

The anthraquinone-1,2,3,4-d_4 (5.0 g) was reduced with tricyclohexyloxide (25 ml of the prepared solution) to yield 0.11 g of purified anthracene-1,2,3,4-d_4 (3%)

Mass spectrum: *m/e* (relative intensity) 181(8.3), 182(111.5), 183(17.6).

N.m.r.: δ 7.46 (s, 2H), 8.02 (m, 2H), 8.42 (s, 2H).

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