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Oxidation of Aliphatic Side Chains in Anthracene Diels-Alder Adducts

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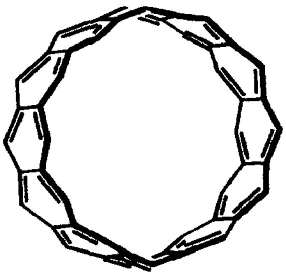
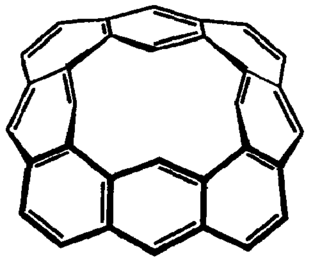
An efficient oxidation of methyl and primary side chains of anthracene Diels Alder adducts with KMnO$_4$ is reported. The oxidation leaves the bridgehead methines intact providing Diels-Alder adducts of anthracenecarboxylic acids. Retro Diels-Alder reaction allows for the preparation of the parent anthracenecarboxylic acids.

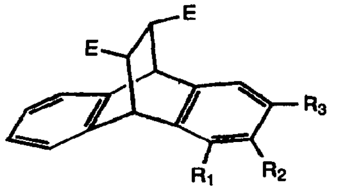
Recently, we have been interested in the synthesis of nonplanar, "cyclic" polyacenes such as **1** and **2**. One of our approaches to these novel hydrocarbons involves iterative homologation of anthracene Diels-Alder (DA) adducts **3** and **4** to the polyDA adducts of **1** and **2**,[1] respectively. The DA adducts serve both to protect the polyacene and to provide the necessary curvature for closure to a "cyclic" polyacene structure. In order to implement this approach, we required a means of oxidizing methyl anthracene DA adducts to the corresponding carboxylic acids *i.e.* conversion of **5** to **3**.



1



2

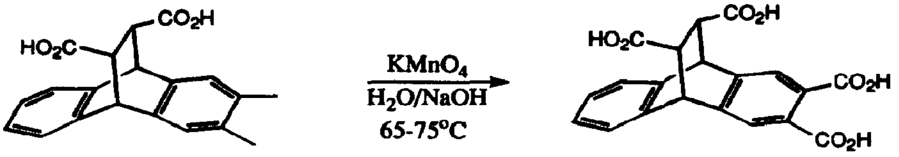


[O] **3** R_1=H, R_2=R_3=CO_2H
4 R_1=R_2=CO_2H, R_3=H
5 R_1=H, R_2=R_3=CH_3

The oxidation of anthracene DA adducts would also provide an important means of preparing anthracene carboxylic acids themselves via retro-DA[2] of the oxidized adduct. Attempted side chain oxidation of polycyclic aromatic hydrocarbons generally results in ring cleavage and/or quinone formation rather than polycyclic aromatic acids.[3,4] Anthracenes in particular tend to yield anthraquinones or anthraquinone carboxylic acids. The DA adduct should protect the 9 and 10 positions of the anthracene nucleus. Although the bridgehead carbons in the DA adduct might also be oxidized, we reasoned that since the bridgehead hydrogen is orthogonal to both aromatic π-systems it is rendered "nonbenzylic", and therefore, unreactive. Since 9 and 10 alkyl substituents would be protected in the DA adduct, selective oxidations would be feasible.

We now report the successful oxidation of fumaric acid/anthracene DA adducts in excellent yield, and the retro-DA reaction of several of the oxidized adducts to provide the parent anthracene carboxylic acids.

We initially examined the oxidation of the unfunctionalized DA adduct 5 (E=CH_3). Due to the insolubility of the adduct in aqueous solution, standard permanganate or chromic acid oxidations failed completely (starting material recovered). Phase transfer catalysis[5] and the use of solutions of tetrabutylammonium permanganate[6] in benzene or pyridine were also unsuccessful. The base soluble fumaric acid adduct , however, was readily oxidized by aqueous $KMnO_4$ at 65-75°C to the corresponding tetracarboxylic acid (eq 1). No oxidation of the bridgehead carbons was observed in this temperature range even in the presence of excess permanganate. At temperatures >80°C some decomposition was observed. It is not known whether this was the result of bridgehead oxidation or ring degradation.

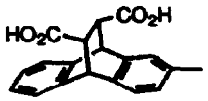
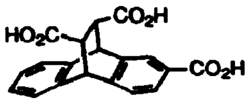
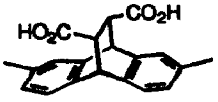
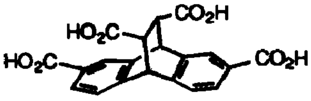
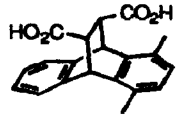
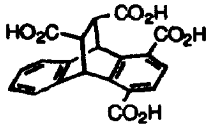
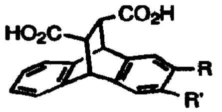
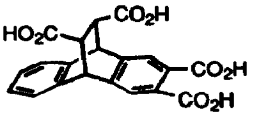
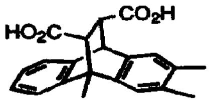
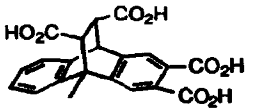
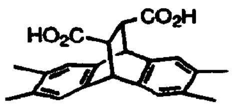
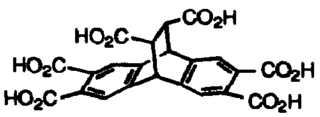
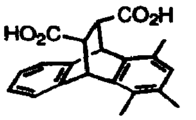
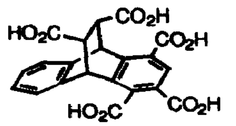
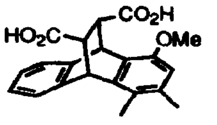
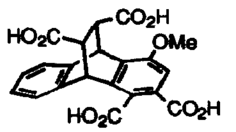
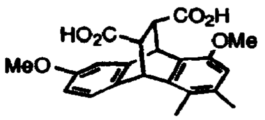
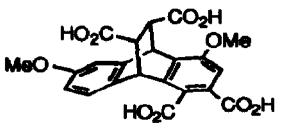


eq 1

The reaction is of wide scope and gives excellent yields with a variety of substituted anthracene DA adducts (see table). As many as four methyl groups have been oxidized (entry 6). There is no problem oxidizing ortho disubstituted compounds (entries 4-9), and three methyl groups in one benzenoid ring were all readily oxidized (entry 7). As expected, a 9-methyl substituent (entry 5) was not oxidized. Oxidation of primary alkyl substituents (entry 4b) was also successful. We presume that secondary substituents would be oxidized as well, but there would not appear to be any advantage in their use. Methoxy groups (entries 8 and 9) did not interfere or result in cleavage of the aromatic ring (which would almost certainly occur in the "unprotected" anthracene[2]). In no instance did the oxidation fail. The products are easily obtained by acidification and extraction with ether.

To demonstrate the utility of the oxidation procedure for the preparation of anthracene carboxylic acids themselves, we examined the retro-DA[2] reaction of several of the oxidation products (see table). The DA adducts were refluxed in phenyl ether (bp 259°C). The liberated fumaric acid was deposited in the reflux condenser so that it was easily separated from the reaction mixture. Upon cooling the liberated anthracene acid (or anhydride, see below) precipitated from the phenyl ether. This simple procedure provided acids of high purity. Because there is no need for flash vacuum pyrolysis, the oxidation/retro-DA procedure is a very convenient means of preparing anthracenecarboxylic acids. Since methylanthracenes (and their DA adducts) are readily obtained, the method should be a useful and general means of preparing carboxylic acids which would be difficult if not impossible to obtain by other means. The preparation of the previously unknown 4-methoxy- and 4,6-dimethoxy- anthracene-1,2-dicarboxylic anhydrides (entries 8 and 9) demonstrates the utility of this procedure.

Table: Oxidation of Fumaric Acid/Anthracene DA Adducts with $KMnO_4$.

entry	DA adduct[a]	oxidation product[b]	yield(%)	retroDA[c]
1			100	84
2			90	-
3			100	-
4	 a R=R'=CH_3 b R,R'=$(CH_2)_4$	 (from 4a and 4b)	a-100 b-100	79[d]
5			89	-
6			50[e]	-
7			93	-
8			92	90[d]
9			88	94[d]

a) For unsymmetrical anthracenes a mixture of the two *trans* diastereomers was used. b) See text for reaction conditions. c) Unoptimized yield (see ref. 6); a "-" indicates reaction was not attempted. d) Isolated as anhydride. e) Product isolation was difficult due to the high water solubility of the hexacarboxylic acid.

General Procedure for the Oxidation of DA Adducts

The reactions were carried out on 100mg to 10g scales. In a typical procedure, the DA adduct (10 mmol) was dissolved in aqueous NaOH (100mL, 0.5N) and warmed to 60°C. A slight excess of potassium permanganate (2.5 eq per methyl group) was then added in 3 to 5 portions (depending on the amount) at 15 minute intervals. The (initially) exothermic reaction caused the temperature to rise slightly to 68-72°C. Note: to avoid overoxidation the temperature should not be allowed to exceed 80°C. After the addition of permanganate was completed, the reaction mixture was maintained at 65-75°C overnight. Ethanol was carefully added to destroy any residual permanganate. The precipitated MnO_2 was reduced by adding an excess of $NaHSO_3$ followed by slow addition of HCl (*Caution* SO_2 gas may be evolved) to give a clear, colorless, homogeneous solution. The solution was acidified further and in some instances (depending on the number and positions of the carboxyl groups) the product precipitated from solution. The aqueous solution was then extracted several times with ether. The organic layers were combined, washed with saturated NaCl solution, and dried over anhydrous Na_2SO_4. The solution was filtered and concentrated *in vacuo*. The oxidation products were obtained as white solids and found to be quite pure by NMR. The proton and carbon spectra were in accord with the structures; disappearance of the methyl resonances and a downfield shift in the bridgehead resonances were particularly diagnostic. GC/MS analysis resulted in retroDA and anhydride formation (from *o*-diacids), but nonetheless, confirmed that oxidation had occurred.

General Procedure for the RetroDA Reaction

The DA adduct (10 mmol) was suspended in phenyl ether (10mL) under an atmosphere of nitrogen. The mixture was brought to reflux (mixture becomes homogeneous) and maintained at reflux for 3-4 h during which time the liberated fumaric acid was deposited on the top of the reaction vessel and in the reflux condenser. The mixture was cooled slightly and then decanted away from any fumaric acid while still warm. A precipitate formed upon cooling to RT. The mixture was filtered, the solid washed twice with CCl_4 and then dried under vacuum. The resulting anthracenecarboxylic acid or anhydride (anhydride formation occurred in refluxing phenyl ether for*o*-diacid) was obtained in very good yield[7] and was found to be quite pure by NMR and GC/MS.

1.) Marquardt, D. J.; McCormick, F. A. Presented at the 33rd National Organic Chemistry Symposium, Montana State University, Bozeman, MT June 13-17, 1993.
2.) Chung, Y. S.; Duerr, B. F.; McKelvey, T. A.; Nanjappan, P.; Czarnik, A. W. *J. Org. Chem.* **1989**, *54*, 1018. Chung, Y. S.; Duerr, B. F.; Nanjappan, P.; Czarnik, A. W. *J. Org. Chem.* **1988**, *53*, 1334.
3.) Hudlicky, *Oxidations in Organic Chemistry*; American Chemical Society: Washington DC, 1990, pp105-109. Lee *The Oxidation of Organic Compounds by Permanganate and Hexavalent Chromium*; Open Court; La Salle IL, 1980, pp43-64.
4.) The successful oxidation of substituted naphthalenes and 2-methyl anthracene by dichromate in a rocking autoclave has been demonstrated: Freidman, L.; Fishel, D. L.; Shechter, H. *J. Org. Chem.* **1965**, *30*, 1453.
5.) Herriott, A. W.; Picker, D. *Tetrahedron Lett.* **1974**, 1511.
6.) Sala, T; Sargent, M. V. *J. Chem. Soc. Chem. Comm.* **1978**, 253.
7.) A small amount of additional, impure acid could be obtained from the mother liquor (not included in the yields).

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