

## THE ANIONIC ALKYLATION OF EASILY REDUCIBLE ARENES. A PHOTOCHEMICAL ROUTE TO NUCLEOPHILIC AROMATIC SUBSTITUTION OF ANTHRACENE BY ORGANOLITHIUMS

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### Summary

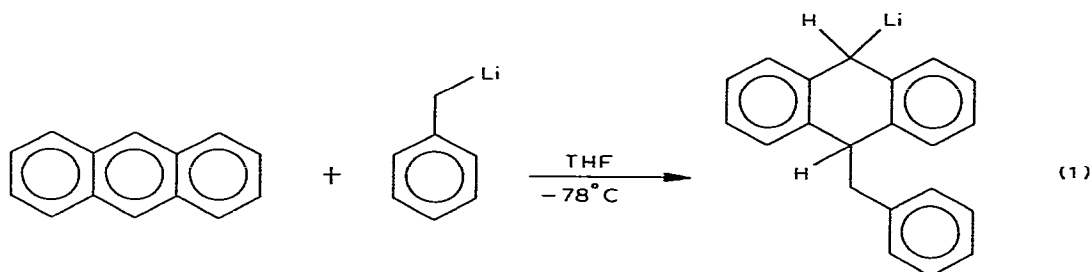
High yield nucleophilic addition ensues upon mixing tetrahydrofuran solutions of benzyllithium or cyclooctadienyllithium and anthracene at low temperatures. At least part of this addition proceeds by a single electron transfer pathway. Photolysis of the resulting adducts leads to the elimination of lithium hydride, giving net nucleophilic substitution in approximately 50% yield. The analogous reaction fails with naphthalene, where photolysis of the organolithium/arene mixture leads to dimeric products derived from the organolithium.

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The known resistance of olefins to nucleophilic attack, together with their ready reactivity with radicals or electrophiles, is easily understandable from simple charge density arguments. Nonetheless, the ability to conveniently accomplish such nucleophilic attacks on electron-rich  $\pi$ -systems would provide a valuable tool for effecting carbon-carbon bond formation. Our interest in photoinduced electron transfer from anions [1] has led us to investigate several photoreactions of arene/resonance-stabilized anion mixtures. We report here our results on the alkylation of anthracene with benzyllithium and cyclooctadienyllithium, examples of typical resonance-stabilized carbanions, as well as preliminary mechanistic inferences regarding the reaction. The products observed constitute formal nucleophilic additions and/or substitutions occurring through a new mechanistic pathway.

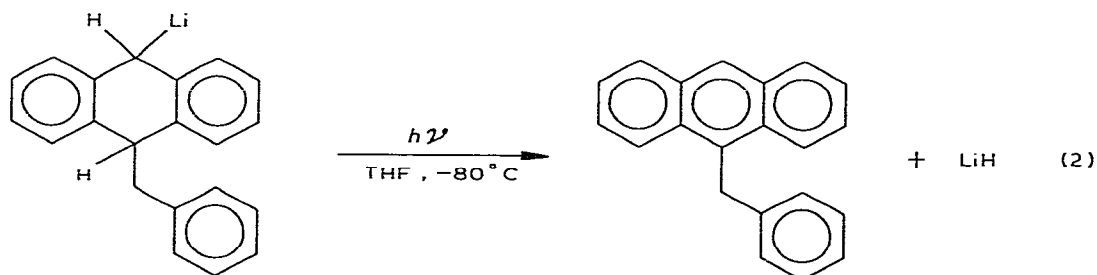
### Results

Upon mixing solutions of benzyllithium [2] and anthracene in tetrahydrofuran (THF) at  $-78^{\circ}\text{C}$ , the intense red color ( $\lambda_{\text{max}}$  450 nm) characteristic of the anion of 9-benzylidihydroanthracene developed, eq. 1. If the reaction were followed at  $-78^{\circ}\text{C}$ , an ESR signal identical to that reported for the anthracene radical anion [3] could be observed as the color continued to intensify. After



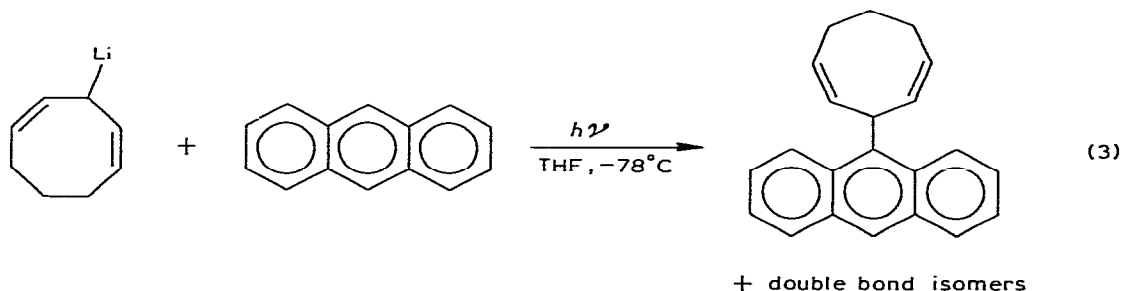
3 h, the ESR signal had decayed and a water workup afforded 9-benzylidihydroanthracene [4], isolable in 80% yield. Small (<10%) quantities of 9,10-dihydroanthracene, 9,9',10,10'-tetrahydro-9,9'-dianthryl, and bibenzyl were also formed.

Photolysis of the red anionic solution at  $-80^{\circ}\text{C}$  with visible or long wavelength ultraviolet light resulted in a slow elimination of lithium hydride, producing 9-benzylanthracene [5] in 47% overall yield, eq. 2. None of this net sub-

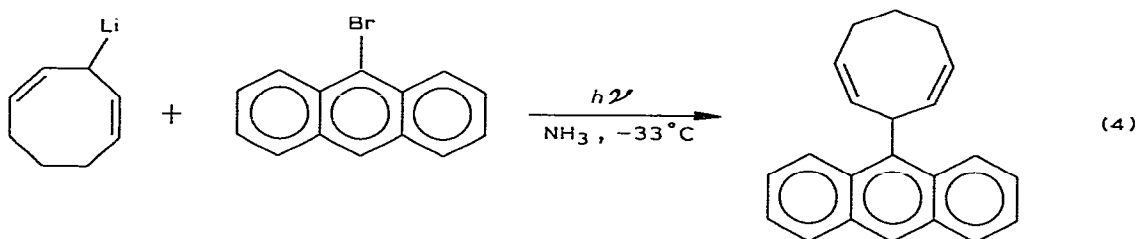


stitution product could be detected in the absence of light. The distribution of products was independent of the excitation wavelength.

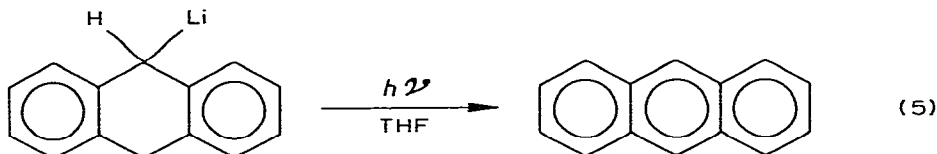
Parallel reactivity could also be observed with cyclooctadienyllithium [6]. Thus, a mixture of double bond isomers ( $\sim 87\%$ ) of 9-cyclooctadienyldihydroanthracene was obtained after an acidic quench of the dark red solution formed upon mixing THF solutions of cyclooctadienyllithium and anthracene at  $-78^{\circ}\text{C}$ . Long wavelength UV photolysis of the anionic mixture resulted in a slow production of 9-cyclooctadienyl anthracenes, eq. 3, a mixture identical to



that obtained from the electron-initiated  $S_{RN}1$  reaction [7] of 9-bromoanthracene with cyclooctadienyllithium, eq. 4.

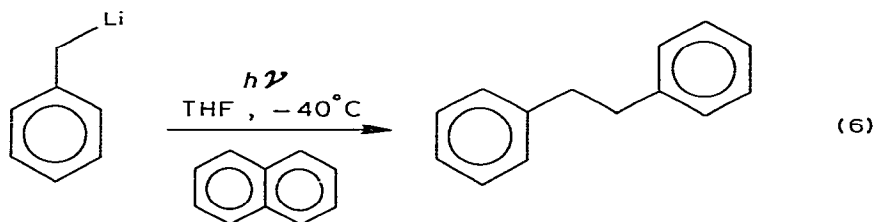


Photolysis of a THF solution of the lithium salt of 9,10-dihydroanthracene at  $-60^{\circ}\text{C}$  at  $350 + 20\text{ nm}$  showed the slow formation of anthracene, eq. 5, but



no additional products could be observed.

Admixture of THF solutions of naphthalene and benzyllithium at  $-78^{\circ}\text{C}$  gave no discernible reaction, but long wavelength UV photolysis of this mixture at  $-40^{\circ}\text{C}$  led to excellent yields of bibenzyl ( $\sim 90\%$ ), with naphthalene and isomeric dihydronaphthalenes representing the sole naphthalene-derived products, eq. 6.



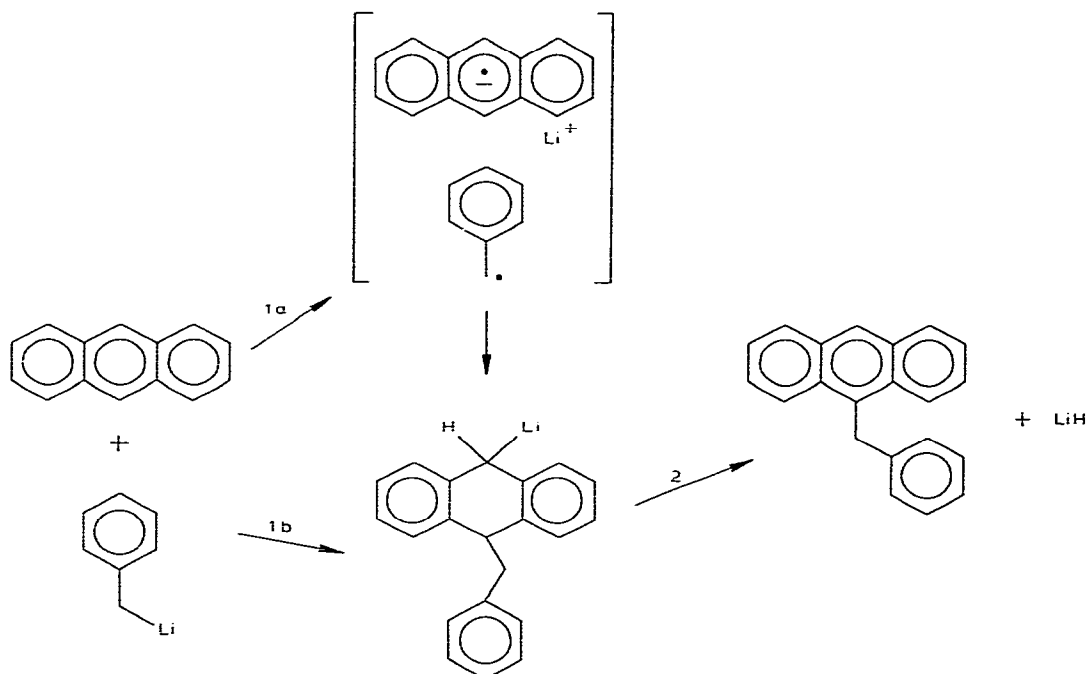
A green color developing during photolysis was identical to that observed for the lithium salt of the naphthalene radical anion in THF [8].

## Discussion

Although a number of studies of thermal arene alkylations using organometallic reagents have been reported [9], relatively poor yields of products formed with minimal regiocontrol are usually obtained. The efficiency of such reactions can be improved by incorporating activating (electron-withdrawing) substituents on the ring [10] or by using special nucleophiles, e.g., sulfonium or sulfoxonium ylides [11], the dimsyl anion, or other sulfoxide or sulfone conjugate bases [12]. The results obtained here show that our goal, to determine whether photoactivation of carbanions might provide a synthetic alternative to these routes, can be realized for selected reaction partners.

We consider specifically the reaction of anthracene with benzyllithium, although exactly analogous reactions are also observed with cyclooctadienyllithium. This nucleophilic substitution proceeds through two distinct stages:

the formation of adduct and the elimination of lithium hydride, Scheme 1.



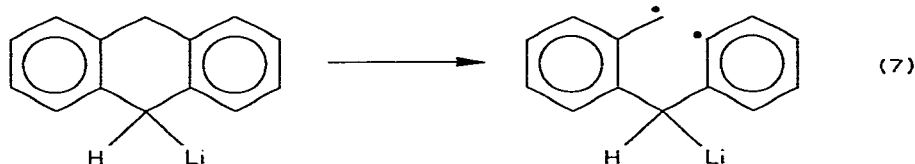
SCHEME 1. Addition-elimination in nucleophilic substitution.

The formation of the radical anion of anthracene upon treatment with benzyl-lithium and its disappearance as the adduct is formed is consistent with at least partial formation of an adduct through a pathway involving single electron transfer, path 1a. Although this process must be at least competitive with more conventional nucleophilic attack, path 1b, we cannot yet estimate how large a fraction of the reaction proceeds through this initial single electron transfer pathway. Trace quantities of bibenzyl and dihydroanthracene observed in the reaction could be explained by leakage of the partners of this radical-radical anion pair from the solvent cage, with coupling or further reduction leading to the observed products. Tetrahydrodianthryl, which we find in trace quantities, is also known to be formed from the anthracene radical anion [20]. ESR evidence for analogous thermal electron transfer from carbanions to electron-poor nitroaromatics has been presented by Russell and coworkers [13].

A consideration of the difference between the oxidation potential of benzyl-lithium ( $-1.4$  V vs. SCE) [14] and the reduction potential of anthracene ( $-1.9$  V vs. SCE) [15], however, predicts that electron transfer should be endothermic by about 12 kcal/mole. A significant contribution from the subsequent exothermic coupling is required therefore if thermal electron transfer routes are to be postulated. The photochemical acceleration of the net substitution may, in part, derive from the shift of this electron transfer equilibria upon generating excited state species. It is interesting to note that thermal adduct formation

appears to be much faster with anthracene-cyclooctadienyllithium ( $E_{pc} -1.7$  V vs. SCE) [1] where this energy difference is lower.

The photochemical elimination of LiH from alkali metal salts of dihydroanthracene finds precedent in spectroscopic studies which suggest the photochemical expulsion of a hydrogen atom from this compound [16]. (In previous work, however, excitation sources with wavelengths shorter than 360 nm have been required.) Our observation of reasonable chemical yields of alkylated arenes is the first, however, to establish that this reaction can have synthetic utility. Furthermore, since no arene cleavage products could be detected, reversible ring cleavage reactions, eq. 7, which have been suggested from spec-



troscopic measurements of the unsubstituted sodium salt [17], apparently do not interfere with net elimination.

Although both the anion and anthracene absorb in the excitation wavelength region employed here, the absence of a dramatic wavelength effect on the observed products upon shifting to longer wavelengths where the adduct is the sole absorber implies that excitation of anthracene is not specifically required for this photoreaction. It should also be noted that the well-known photodimerization of anthracene [18] is completely inhibited in the presence of these resonance-stabilized anions and that the products observed here (exclusively 9-substitution) are not consistent with free radical attack on neutral anthracene, where di- and tri-benzylated and benzylated coupling products are observed [19].

The photoreactions of the benzyllithium/naphthalene mixture are dramatically different than those described above. That the addition/elimination sequence is much slower in this system can be explained in several possible ways. Conventional nucleophilic attack could be slower because of the formation of a less highly stabilized anionic intermediate. Alternatively, the greater difference in redox potentials between naphthalene ( $E_{pc} -2.5$  V vs. SCE) [15] and benzyllithium could completely inhibit the first step required for addition. Finally, the coupling of a benzylic radical with benzyllithium could have become more favourable than in-cage collapse of the radical-radical anion pair. Although the green color characteristic of the naphthalene radical anion is observable, no clear evidence for its involvement along the reaction pathway to bibenzyl has yet been garnered. Its potential role as a redox catalyst for oxidative coupling reactions is under further investigation in our group.

Our results can be compared with previous photolyses of anthracene in the presence of organolithiums. With phenyllithium, nearly no C—C bond formation could be detected, although reasonable quantities of reduction products and biphenyl were formed [20]. With simple alkylolithiums (n-butyllithium or methylolithium), reductive alkylation products are formed, although in significantly lower yields than reported here [21,22]. Better regiocontrol is also observed with our stabilized organolithiums than with methylolithium where sub-

stantial attack at the 2-position is also observed [22]. In all these cases, spectral studies have shown substantial aggregation of the organolithium [23]. In contrast, both benzyllithium [23] and cyclooctadienyllithium [24] exist as monomers in THF and both represent stabilized systems in which there is substantial ionic character in the carbon–lithium bond. While we cannot yet conclusively discuss the relative importance of these two factors, our results suggest that effective alkylation can be achieved for at least some anion-arene pairs.

## Experimental

*General.* Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Proton nuclear magnetic resonance (nmr) spectra were obtained on a Varian 390 spectrometer, with chemical shifts reported in ppm downfield from tetramethylsilane (internal standard). Gas chromatography-mass spectroscopy (GC/MS) analyses were performed on a Finnigan 4023 automated GC/MS equipped with an INCOS data system for matching an extensive library of standard fragmentation patterns. Low resolution mass spectra were obtained with a Dupont 21-491 mass spectrometer. Ultraviolet spectra were recorded on a Cary 14 spectrometer and electron spin resonance (esr) spectra were obtained on a Varian E-9 EPR spectrometer equipped with a Varian E-101 microwave bridge. Gas-liquid phase chromatography (glpc) was conducted on a Varian Aerograph 920 instrument with a thermal conductivity detector or on an Antek 400 instrument equipped with a flame ionization detector. High pressure liquid chromatography was conducted on a Waters R-401 LC system.

Tetrahydrofuran (THF) was freshly distilled from potassium or from benzophenone ketyl.

*Reaction of benzyllithium with anthracene.* Benzyllithium (0.01 mol in 50 ml of THF, prepared by metallation of toluene with sec-butyllithium [2]) was added to a 50 ml THF solution of anthracene (.178 g, 0.01 mol) at  $-78^{\circ}\text{C}$  under an argon atmosphere. A red color was detected immediately, which intensified over a 3 h period of stirring at  $-78^{\circ}\text{C}$ . Aliquots were removed immediately upon mixing and at variable time intervals during the reaction period for ESR analysis. A signal with a  $g$  value and hyperfine splitting pattern identical to that reported [3] for the anthracene radical anion could be detected immediately. The intensity of the signal grew, plateaued, and decreased, nearly disappearing, over the 3 h period. The mixture was then allowed to come to room temperature and was decomposed by the addition of 10 ml of water. The ether layer was dried over sodium sulfate and the solvent was removed under rotary evaporation. Upon crystallization from petroleum ether, 9-benzyl-9,10-dihydroanthracene [4] (2.16 g, 80%) was obtained: NMR ( $\text{CDCl}_3$ )  $\delta$  7.2 (m, 13 H), 4.2 (t,  $J$  6 Hz, 1 H), 3.6 (s, 2 H), 2.7 (d,  $J$  6 Hz, 2 H); m.p.  $115^{\circ}\text{C}$  (lit. [4]  $115^{\circ}\text{C}$ ).

*Photolysis of 9-benzyl-10-lithio-dihydroanthracene.* The benzyllithium/anthracene mixture described above was transferred to a Pyrex tube for irradiation under an argon atmosphere in the cavity of a Rayonet Photochemical Reactor equipped with  $350 \pm 20$  nm phosphor-coated low pressure mercury lamps. External cooling was provided during the irradiation by suspending the

tube in a thermostatted ( $-60^{\circ}\text{C}$ ) unsilvered Pyrex dewar flask in which the temperature was maintained with a Flexicoil refrigerated cold finger. The photo-reaction was monitored by analyzing 2 ml aliquots by GLPC. After 40 h, the reaction mixture was removed from the photolysis apparatus, allowed to warm to room temperature, and quenched with water. The mixture was separated by using thermal gradient sublimation. The major product was 9-benzylanthracene (1.18 g, 47%), ms:  $m/e$  268 ( $P$ ), 191 ( $P$ -benzyl); NMR ( $\text{CDCl}_3$ )  $\delta$  7.3–8.9 (m, 14 H), 5.0 (s, 2 H)ppm; m.p.  $135^{\circ}\text{C}$  (lit. [19]  $136^{\circ}\text{C}$ ). Minor quantities (<10%) of dihydroanthracene, bibenzyl, 9,9',10,10'-tetrahydro-9,9'-dianthryl, and anthraquinone were identified by comparison of their GC/MS relative retention volumes with known samples of these compounds (50 m SE-30 fused capillary column,  $150^{\circ}\text{C}$ ) and/or matching of their fragmentation patterns with those of the appropriate compound.

In a dark control reaction (identical treatment of the sample except that it was covered with foil during the irradiation), 9-benzyl-9,10-dihydroanthracene was isolated in 80% yield. No 9-benzylanthracene could be detected.

A parallel reaction using a medium-pressure mercury arc filtered (Corning 3-74 yellow cutoff filter) to remove all excitation wavelengths shorter than 400 nm gave identical results except that the rate of conversion was much slower.

*Reaction of cyclooctadienyllithium with anthracene.* Cyclooctadienyllithium [6] in 50 ml THF was added to a solution of anthracene (1.8 g, 0.01 mol) in 50 ml THF under argon at  $-78^{\circ}\text{C}$ . An immediate burst of intense red color developed. No changes in the color could be observed over a 1.25 h period. The reaction mixture was quenched at  $-78^{\circ}\text{C}$  by the addition of 10 ml of saturated ammonium chloride. The ether layer was dried over sodium sulfate and the solvent was removed. Repeated attempts at purification (GLPC, normal and reverse phase high pressure liquid chromatography, sublimation) yielded a mixture of double bond isomers of 9-cyclooctadienyl-9,10-dihydroanthracene, 2.5 g oil (89%): ms ( $m/e$ ) 286 ( $P$ ); NMR ( $\text{CCl}_4$ )  $\delta$  7.1 (br s, 8 H), 5.5 (m, 3.8 H), 3.8 (m, 2 H), 3.7 (d,  $J$  6 Hz, 1 H), 1.0–2.0 (m, 7.2 H)ppm. That only the 9-substituted isomer was present in the mixture was established by subjecting 1 g of this oil to oxidation (heating under reflux with 1 equiv. of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) for 15 min in benzene). The reaction mixture was extracted with aqueous base before the solvent was removed from the organic layer. The resulting mixture gave an identical GLPC trace to that obtained for 9-cyclooctadienylanthracene (vide infra).

*Photolysis of 9-cyclooctadienyl-10-lithio-9,10-dihydroanthracene.* The cyclooctadienyllithium/anthracene mixture described above was transferred to a Pyrex tube for irradiation at  $-70^{\circ}\text{C}$  in the apparatus described above. After a parallel workup, GLPC analysis ( $180^{\circ}\text{C}$ ,  $3' \times 1/4''$  5% SE-30 on firebrick column) indicated the formation of an approximately 50/50 mixture of 9-cyclooctadienyl-9,10-dihydroanthracene double bond isomers and 9-cyclooctadienylanthracene double bond isomers.

*Preparation of 9-cyclooctadienylanthracenes.* A vacuum-insulated three-neck round bottom Pyrex flask equipped with a dry ice/isopropyl alcohol condenser, an overhead stirrer, and an inlet for maintaining a slow stream of dry nitrogen was charged with 150 ml of liquid ammonia. 1,4-Cyclooctadiene (3.2 g, 0.03 mol) and lithium amide (0.7 g, 0.03 mol) were added and the red-orange color

of cyclooctadienyllithium developed as the solution was stirred for 30 min. The apparatus was inserted in the cavity of a Rayonet Photochemical reactor equipped with phosphor-coated (350 + 20 nm) low pressure mercury lamps. The mixture was irradiated as 9-bromoanthracene (7 g, 0.032 mol) was added. After 2 h, irradiation was stopped, 100 ml THF and 10 ml of saturated  $\text{NH}_4\text{Cl}$  was added, and the ammonia was allowed to slowly evaporate. The organic layer was concentrated by partial removal of the solvent under rotary evaporation and the residue was analyzed by GC/MS. A roughly 80/20 mixture of 9-cyclooctadienylanthracene (*m/e*: 284; NMR ( $\text{CCl}_4$ )  $\delta$  7–8 (m, 9 H), 5.4–5.8 (m, 4 H), 1–2.4 (m, 7 H)ppm and 9-cyclooctadienyl-9,10-dihydroanthracene (vide supra) was observed. Although it was possible to separate the anthracene derivatives from their dihydro relatives with repeated passes through a preparative GLPC column (150°C, 3'  $\times$  1/4" 5% SE-30 on firebrick), purification of the double bond isomers proved impossible because of extensive polymerization accompanying all attempted separation techniques.

*Photolysis of a benzyllithium/naphthalene mixture.* Benzyllithium (0.01 mol) in 50 ml THF was added to a solution of naphthalene (1.36 g, 0.01 mol) in 50 ml THF at  $-60^\circ\text{C}$ . No apparent reaction could be detected. After 30 h, the reaction mixture was quenched with water and the organic residue obtained after removal of solvent was analyzed by GLPC. Only naphthalene and toluene were present. No bibenzyl could be detected.

A second benzyllithium/naphthalene mixture was irradiated at  $350 \pm 20$  nm in the photoreactor described above. Usual work-up gave, after separation by thermal gradient sublimation, naphthalene (1.3 g, 95% recovery) and bibenzyl (0.8 g, 88%). The latter was identified by comparison of its spectral and chromatographic properties with an authentic sample of bibenzyl.

*Photolysis of 9-lithio-9,10-dihydroanthracene.* 9,10-dihydroanthracene (1.8 g, 0.01 mol) in THF (10 ml) was treated with *sec*-butyllithium (0.01 mol) at  $-60^\circ\text{C}$ . The resulting mixture was irradiated in the previously described apparatus at  $350 \pm 20$  nm for 40 h at  $-60^\circ\text{C}$ . A water quench of the reaction mixture, followed by the usual work-up, gave 1.7 g of a solid, GLPC(5' 5% QF-1 on Chromosorb W, 150°C) analysis of which indicated the presence of anthracene (11%) and dihydroanthracene (89%). No anthracene could be detected in a parallel thermal control reaction.

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