to Prof. J. A. Retamar for his permanent interest and support of this work. Financial support from the National Research Council (CONICET) and the Science and Technology Secretariat (SUBCYT) of Argentina is also deeply acknowledged. GLC–MS determinations and elemental analyses were performed by UMYMFOR (FCEN-CONICET).

Registry No. 1, 546-80-5; 2, 471-15-8; 3, 88904-61-4; 4, 88904-62-5; 5, 88904-63-6; 6, 88904-64-7; 7, 88930-40-9; BuLi, 109-72-8; PhLi, 591-51-5.

Metal–Ammonia Ring Reduction of Aromatic Carboxylic Acid Esters

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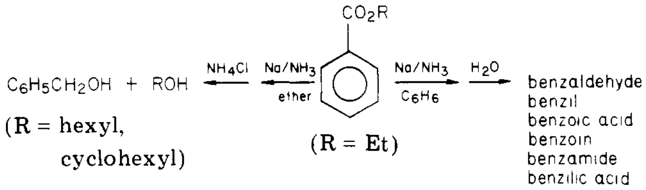
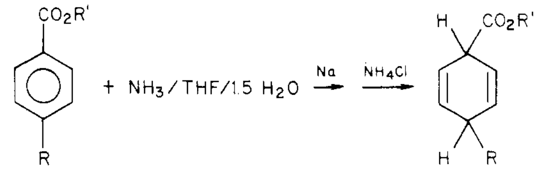
Although esters are often reduced to alcohols with metal–ammonia solutions, it has been found that aromatic carboxylic acid esters can be reduced efficiently to the corresponding dihydro aromatics when 1.25 equiv of water is present before metal addition. The general effect of the presence of water (before metal addition) upon metal–ammonia reduction of polycyclics was tested with anthracene (0.5 g), which was reduced to 9,10-dihydroanthracene (97% yield) in the presence of 3.5 g of water. Polynuclear aromatic esters are reduced smoothly by this technique, but in the absence of water, alkyl 9-anthroates gave a dimer assigned as axial/axial on the basis of nuclear Overhauser enhancements. Possible mechanistic pathways for dimer formation were investigated by the addition of 9,10-dihydroanthracene monoanion as well as anthracene dianion to ammonia/THF solutions of ethyl anthroate. This led to dimer and trimer formation, respectively. The structures of these compounds are discussed in light of their carbon and proton NMR spectra.

The reduction of esters to alcohols by alkali metals and alcohol in liquid ammonia is a familiar process known as the Bouveault–Blanc procedure.[1a] These same reagents, under appropriate conditions, can also effect the ring reduction of aromatic compounds in a useful reaction generally known as Birch reduction.[1] Hence treatment of aryl carboxylic acid esters with metal/ammonia solutions is potentially complex. In fact, Kharasch et al.[2] investigated the reaction of ethyl benzoate with $Na/NH_3/C_6H_6$ and found a variety of products all involving reduction of the carbonyl group and/or cleavage of the alkyl portion of the ester. Moreover, the presence of benzamide suggests susceptibility of the carbonyl group to nucleophilic attack by ammonia (or amide) in addition to reduction processes. More recently, the efficient (78–97% isolated yields) conversion of several different benzoate esters to alcohols using sodium/ammonia solutions has also been reported.[3]



In view of these results, the ring reduction of aryl carboxylic acid esters appeared quite challenging but nonetheless was of interest to us since (1) we have found dihydroaromatic esters to be more resistant to isomerization, rearomatization, etc., than the corresponding acids and (2) we hoped that the carboalkoxy group might show enhanced activation properties, since acids are necessarily present as carboxylate anions in ammonia solution providing an additional negative charge. Not unexpectedly, our initial experiments with benzoate esters met with failure. However, in a somewhat serendipitous manner we found that ring reduction of ethyl benzoate can be effected almost quantitatively when water (ca. 1.5 equiv) is present *before* the addition of metal.[4] This is, of course, rather unusual since metal/ammonia reductions are usually carried out with the rigorous exclusion of water, although alcohols are often used as cosolvents for the reduction of benzene derivatives.[1] Generally, we have not found alcohols to be as satisfactory as water, but, in any event, the key to our procedure is the presence of the proton source *before* the addition of metal.



R = H, Me; R′ = Et, *t*-Bu

Electron addition to the benzoate esters must occur much faster than destruction of the metal by water since we employ only a slight excess of sodium. The likely role of the water is rapid protonation of the radical anion 1 before such processes as dimerization or ester cleavage may occur. The (delocalized) anion 2 appears resistant to further electron addition as well as reaction with any nucleophiles that may be present. Similarly, the starting esters are unaffected by liquid ammonia (at least for short

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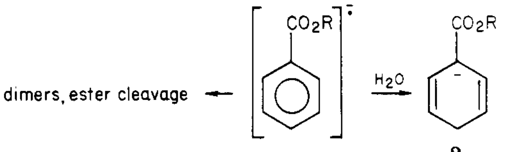
(1) (a) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin, Inc.: Menlo Park, CA, 1972; pp 150–151. (b) Birch, A. J.; Subba Rao, G. "Advances in Organic Chemistry, Methods and Results"; Taylor, E. C., Ed.; Wiley-Interscience: New York, 1972. (c) Smith, H. "Chemistry in Nonaqueous Ionizing Solvents"; Jander, G., Spandan, H., Addison, C. C., Eds.; Interscience: New York, 1963; Vol. I, p 2. (d) Harvey, R. G. *Synthesis* **1970**, 161.

(2) Kharasch, M. S.; Sternfeld; Mayo, F. R. *J. Am. Chem. Soc.* **1940**, *62*, 362.

(3) Pinnick, H. W.; Fernandez, E. *J. Org. Chem.* **1979**, *44*, 2810.

(4) For a preliminary report, see: Rabideau, P. W.; Huser, D. L.; Nyikos, S. J. *Tetrahedron Lett.* **1980**, *21*, 1401.



1 2

periods at −78 °C), and the reaction mixtures are inverse quenched[5] into aqueous ammonium chloride to minimize contact with strong base during the quenching process.

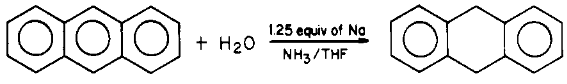
Since this reaction involves an internal competition between the carbonyl group and the aromatic ring, we felt that a large ester function (e.g., *tert*-butyl) might block chemistry at the carbonyl group and better promote ring reduction (although any cleavage processes that produce R· would be enhanced). In fact, we do prefer the *tert*-butyl esters although we have also obtained satisfactory results with ethyl esters. Methyl esters, however, have not provided good results. We were also interested in the effect of *p*-alkyl groups, since (1) this might shift electron density toward the carbonyl group, and (2) protonation at an alkyl substituted position is considered to be slower.[1b] Reduction of *p*-methylbenzoate proceeded well, producing a mixture of cis and trans 1,4-dihydro products.[5] However, *p*-ethyl-, *p*-isopropyl-, and *p*-*tert*-butyl-substituted *tert*-butylbenzoates did not afford any significant amount of ring-reduced products but rather resulted mainly in aldehyde formation.

Our premise has been that electron addition can be a faster process than reaction of the sodium with water. If true, other compounds with sufficiently high electron affinity should also show this behavior.[6] We should note that Wooster[6c] examined the reduction of toluene in the presence of water in 1937 and reported "a highly unsaturated liquid product which boils over the range 111–115°, chars with fuming sulfuric acid, reacts vigorously with liquid bromine and rapidly decolorizes a solution of bromine in carbon disulfide." However, we have reexamined this reaction with varying amounts of water, and NMR analysis indicates the reaction mixture to be primarily toluene with small amounts of reduction products, only a part of which appears to be 1-methyl-1,4-cyclohexadiene. Hence, toluene is not a case in point. On the other hand, anthracene has a relatively high electron affinity and we chose to investigate its reduction behavior in the presence of water (eq 1). We found that an *extraordinarily* large excess of water (i.e., 75 equiv) could be present before metal addition with little effect on the yield of 9,10-dihydroanthracene (relatively large volumes of NH_3/THF were used to minimize solubility effects). Hence, *in some cases*, it is not important that the ammonia and cosolvent be completely anhydrous for successful reduction. Anthracene is a particularly good case since any actual 9,10-dihydroanthracene formed in situ before the final quench will not itself be reduced under these conditions (i.e., absence of alcohols), since it contains only isolated benzene rings.[1]

Table I. Metal-Ammonia Reduction of Alkyl 9-Anthroate[a]

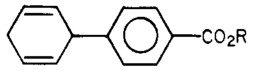
alkyl group	metal	cosolvent	concn, M	ratio[b] monomer/dimer
Et	Na[c]	THF	0.025	38:62
Et	Na[c]	THF	0.04	36:64
Et	Na[c]	THF	0.05	31:69
Et	Na[c]	THF	0.1	18:82
Et	Na[d]	ether	0.05	25:75
Et	Na[e]	THF	0.05	41:59
t-Bu	Na[c]	THF	0.05	44:56
t-Bu	Na[e]	THF	0.05	58:42
Et	Li[d]	THF	0.05	45:55[f]
Et	K[d]	THF	0.05	43:57

[a] Reactions carried out under anhydrous conditions at −33 °C for 20 min and inverse quenched. [b] Determined from NMR integrations. [c] Metal added last. [d] Ester added last. [e] Ester added last over a 15-min period. [f] Plus some unidentified products.

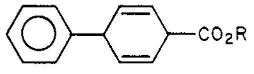


0.5 g 3.5 g 97% (1)

We have previously reported a particularly useful application of this reaction involving biphenyl-4-carboxylic acid. Metal/ammonia reduction of the parent acid **3** (R = H) provides, according to one report,[8] two dihydro acids (**3** and **4a**) together with 25% neutral products, and, according to a second report,[7] only the two dihydro acids in a 1:3 ratio (respectively). In view of this variety of products, it is significant that *tert*-butyl biphenyl-4-carboxylate affords only the single product **4b**. Hence, complete regiospecificity can be achieved by use of the ester functionality in this case. Presumably, the ester group is more activating than carboxylate due to the absence of the additional negative charge on oxygen.

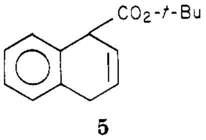


3, R = H



4a, R = H
b, R = *t*-Bu

We wanted to apply these methods to fused, polynuclear systems, and so investigated the reduction of *tert*-butyl 1-naphthoate as well as ethyl and *tert*-butyl 9-anthroate.



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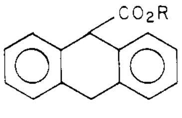

6, R = *t*-Bu
7, R = Et

These polynuclears reduced smoothly in the presence of 1.5 equiv of water to produce the dihydro esters **5** and **6**. However, since these systems are more highly delocalized than the benzoates, we questioned the need for added water and decided to try anhydrous conditions. Interestingly, although ethyl 9-anthroate provides only **7** in the presence of water added before metal addition, a new product (50–75% yield) resulted under the anhydrous conditions (see Table I). From the mass spectrum, it was clear that dimerization had occurred, and, at about that

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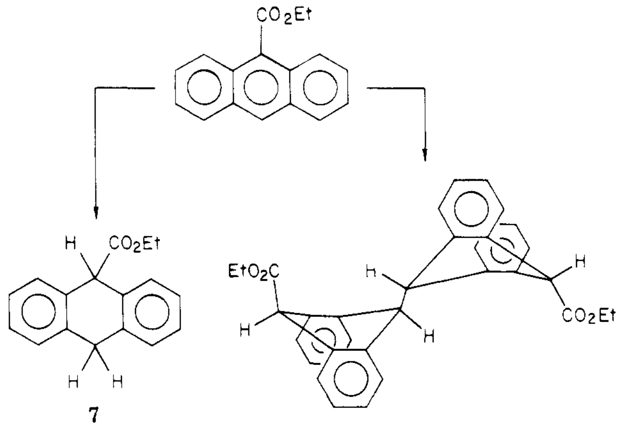
(5) The stereochemical considerations of these reactions is a subject under current investigation in our laboratories.

(6) (a) Van Bekkum et al. studied the reduction of a large number of benzoic acids with lithium–ammonia, and they reported that water is the preferred proton donor with cases involving a 4-alkyl substituent (lithium is of course, much less reactive toward water than sodium). Van Bekkum, H.; Van Den Bosch, C. B.; Van Minnenpathius, G.; DeMos, J. C.; Van Wijk, A. M. *Recl. Trav. Chim. Pays-Bas* **1971**, 90, 137. (b) In a report concerning the metal/ammonia reduction of acetophenone under a wide variety of conditions, one experiment was performed with water present before metal addition in the case of lithium. However, a variety of products were obtained with little ring reduction. Narisad, M.; Wanatabe, F. *J. Org. Chem.* **1973**, 38, 3887. (c) Wooster, C. B.; Godfrey, K. L. *J. Am. Chem. Soc.* **1937**, *59*, 596.

(7) Rabideau, P. W.; Nyikos, S. J.; Huser, D. L.; Burkholder, E. G. *J. Chem. Soc., Chem. Commun.* **1980**, 210.

(8) Franks, D.; Grossel, M. C.; Hayward, R. C.; Knutsen, L. J. S. *J. Chem. Soc., Chem. Commun.* **1978**, 941.

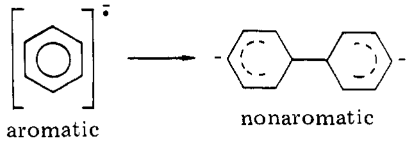


7

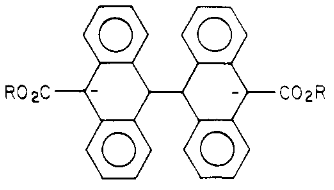
8 (50–75%)

time in our investigation, Kirrstetter and Vagt[9] reported that treatment of methyl 9-anthroate with lithium naphthalenide also afforded a dimer. They did not, however, provide any structural analysis or comment on stereochemical possibilities. The ^{13}C NMR spectrum of 8 showed only six different aromatic carbons, indicating a significant amount of symmetry. In addition, the pseudoaxial preference of substituent groups is well established for 9,10-dihydroanthracenes[10] (especially for large substituents), and so the two units must be joined in a pseudoaxial/pseudoaxial fashion. The appearance of a single C=O resonance in ^{13}C NMR, as well as a single ethyl group in ^{1}H NMR, indicates that both carbethoxy groups must be in the same positions (i.e., either pseudoxial or pseudoequatorial). Irradiation of the (ortho) aromatic protons produced an increase in the integrated intensity of $H_9H_{9'}$ in the proton NMR spectrum, affording a nuclear Overhauser enhancement of ca. 15%. Hence, H_9 and $H_{9'}$ can be assigned as pseudoequatorial, which means the ester groups are pseudoaxial. This is expected to be the most stable arrangement.[10]

Actually, dimerization of aryl radical anions is rare and somewhat controversial. In a review,[11] Holy points out that an early report of anthracenide dimerization followed by carboxylation was later challenged. For this reason and others, Holy expresses skepticism about a later report also suggesting dimerization of photolytically generated anthracenide at high concentrations (yield not reported).[12] More recently, Cho and Harvey[13] reported a small amount (3%) of dimer formation in some silated anthracenes. Failure to commonly observe such dimerizations is not surprising; however, since as Dewar has pointed out,[14] the radical anion is aromatic whereas the dimer is nonaromatic (eq 2). In the case herein, dimer formation can be more easily rationalized due to the increased stability of the dimeric dianion 9 by the presence of the carboalkoxy groups, as well as to the relative lack of aromaticity for the central ring in anthracene.



(2)



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Dimer formation via radical anions could occur in two ways: (a) the simple dimerization of two radical anions (eq 3) or (b) the interaction (electron transfer) between a dianion and neutral ethyl anthroate to produce a pair of radical anions which then combine [eq (4)].[15] However,

$$2[AnCO_2R]^{-\cdot} \rightarrow [RO_2CAnAnCO_2R]^{2-} \quad (3)$$

$$[AnCO_2R]^{2-} + AnCO_2R \rightarrow 2[AnCO_2R]^{-\cdot} \quad (4)$$

$$[HAnCO_2R]^{-} + AnCO_2R \rightarrow [RO_2C(H)AnAnCO_2R]^{-} \quad (5)$$

$$[AnCO_2R]^{2-} + AnCO_2R \rightarrow [RO_2CAnAnCO_2R]^{2-} \quad (6)$$

anthracene itself is known to undergo conjugate additions with certain anions (e.g., *tert*-butyllithium,[16] cycloheptatrienyl potassium[17]) to produce 10-R-9-M derivatives, and this type of process should be enhanced wth ethyl anthroate due to the extra stabilization of the negative charge by the carbethoxy group. Hence we must consider two additional possibilities. Either a monoanion (eq 5) or a dianion (eq 6) could "add across" ethyl anthroate. In the former case, a monoanion could be present as the result of the (mono) protonation of ethyl anthroate dianion (this process has been established for anthracene itself[18]). However, in such a case one would expect to produce the monoanion with charge at C-9 leading eventually to a head-to-tail dimer, not the tail-to-tail dimer as observed. We should also note that eq 4 and 5 may not really be different in that the conjugate addition could proceed by an electron-transfer process.

In any event, we wanted to investigate the possibility of conjugate additions by generating the monoanion and dianion in question and then adding them to ethyl anthroate NH_3/THF solutions. Unfortunately, proton abstraction from ethyl 9,10-dihydroanthroate to produce mono- and dianions did not proceed well, presumably due to the carbonyl function, and so we decided to use unsubstituted 9,10-dihydroanthracene as a model. This produced interesting results. The monoanion was generated by deprotonation with *n*-butyllithium in THF at 0 °C and then added to a solution of ethyl anthroate in NH_3/THF at −33 °C. The major reaction was, in fact, addition to produce the dimer 10 (after quenching with aqueous ammonium chloride). A secondary process appears to be hydride transfer from the monoanion to ethyl anthroate resulting in anthracene formation plus reduced ethyl anthroate. This does not seem unreasonable since the monoanion of 1,4-cyclohexadiene transfers a hydride to 1,3-cyclohexadiene, producing benzene and cyclohexene.[19]

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(9) Kirrstetter, R. G. H.; Vagt, U. *Chem. Ber.* **1981**, *114*, 630.

(10) For a review of the conformational analysis of dihydroanthracenes, see: Rabideau, P. W. *Acc. Chem. Res.* **1978**, *11*, 141.

(11) Holy, N. L. *Chem. Rev.* **1974**, *74*, 243.

(12) Winkler, H. J. S.; Winkler, H. *J. Org. Chem.* **1967**, *32*, 1695.

(13) (a) Cho, H.; Harvey, R. G. *J. Org. Chem.* **1975**, *40*, 3097. (b) These workers also produced dimers by the coupling of 9,10-dihydroanthracenyl radicals formed by oxidation of monoanions. Cho, H.; Harvey, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 2434.

(14) Dewar, M. J. S.; Dougherty, R. C. "The PMO Theory of Organic Chemistry"; Plenum Press: New York, 1975; p 532.

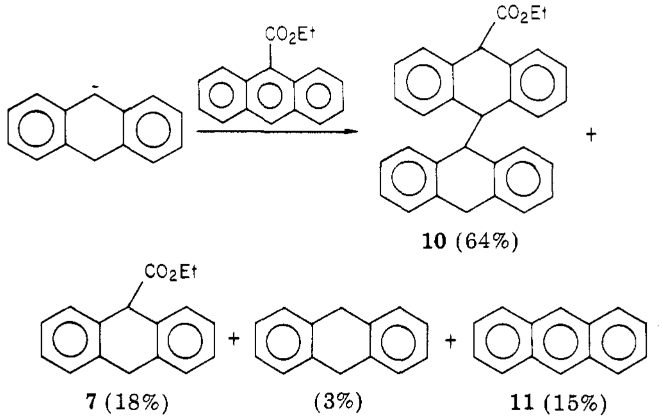
(15) Szwarc, M., Ed. "Ions and Ion Pairs in Organic Reactions"; Wiley-Interscience: New York, 1974.

(16) Harvey, R. G.; Davis, C. C. *J. Org. Chem.* **1969**, *34*, 3607.

(17) Kaupp, G.; Gruter, H.-W.; Teufel, E. *Chem. Ber.* **1982**, *115*, 3208.

(18) Rabideau, P. W.; Burholder, E. G. *J. Org. Chem.* **1978**, *43*, 4283.

(19) Paul, R.; Tchelitcheff, S. *C.R. Hebd. Seances Akad. Sci.* **1954**, *239*, 1222.

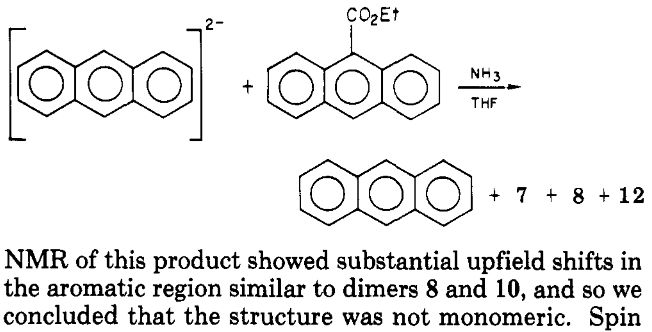


10 (64%)

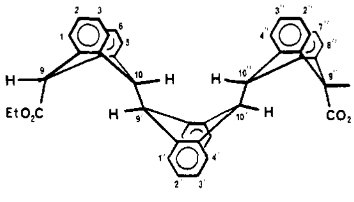
7 (18%) (3%) 11 (15%)

The identification of **10** was unambiguous. As with the dimer, the aromatic proton resonances appeared over a wide range (6.0–7.5 ppm) with two doublets at 6.1 and 6.3 assigned as the "inside" ortho protons H_4H_5 and $H_{1'}H_{8'}$ (not necessarily in that order). The ^{13}C NMR spectrum showed 12 separate aromatic carbons, including four assigned as quaternary due to low intensity. The upfield portion of the spectrum showed six lines that produced the expected multiplicities in the coupled spectrum. This is especially important for the bridging carbons, since doublets at C-9, C-10, and C-9′ together with a triplet at C-10′ clearly establish the proposed structure. Once again, the location of the carbethoxy group was determined by nuclear Overhauser enhancement. Irradiation of the (downfield) aromatics produced a 17% increase in the integrated intensity of H-9. Hence, H-9 is pseudoequatorial and the carbethoxy group is pseudoaxial.

A dianion was generated by the reaction of 9,10-dihydroanthracene with 2 equiv of *n*-butyllithium in THF at 0 °C to produce the characteristic purple color.[13b] Furthermore, addition of ethyl bromide to this reaction mixture produced *cis*- and *trans*-9,10-diethyl-9,10-dihydroanthracenes, confirming the presence of a dianion. Addition of this dianion solution to ethyl anthroate in THF/NH_3 produced a variety of products, suggesting that electron transfer from the anthracene dianion to ethyl anthroate easily competes with protonation by ammonia.[18] Reverse-phase HPLC indicated 45% anthracene, 11% ethyl 9,10-dihydroanthroate (**7**), 11% dimer **8**, and 33% of a compound not previously encountered. The proton NMR of this product showed substantial upfield shifts in the aromatic region similar to dimers **8** and **10**, and so we concluded that the structure was not monomeric. Spin decoupling of the overlapping ethyl CH_2 uncovered an AB pattern for one set of methine protons with the other set, adjacent to the carbonyl, appearing as a singlet. The coupling constant (10.5 Hz) of the AB pattern as well as its ratio to the methine singlet (2:1) indicated a trimer (**12**). This assignment could be confirmed by ^{13}C NMR in the following manner. (1) The trimer **12** exhibits three different quaternary aromatic carbons as observed and confirmed by off-resonance decoupling. (2) There is a single carbonyl carbon resonance. (3) There are three different methine carbons (showing doublets in the coupled spectrum). (4) There is a single ethyl group resonance (showing a triplet and quartet in the coupled spectrum).

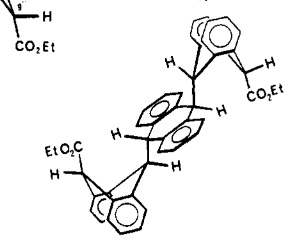


The pseudoxial position of the ester substituents was established by the observation of a ca. 15% nuclear Overhauser enhancement at $H_9(H_{9''})$ when the adjacent aromatic protons were irradiated. However, this technique does not allow for distinguishing between a cis and trans arrangement of the inner ring. However, we have tentatively made an assignment on the basis of proton chemical shift trends using dimer **8** as a model.



CIS 12

TRANS 12



Let us consider a cis isomer and the expected changes in chemical shift for the "inside" ortho protons H_4,H_5 and $H_{4''}$,$H_{5''}$ of the outside rings relative to the dimer **8**. Molecular mechanics calculations[20] as well as NMR data[21] on *cis*-9,10-dialkyl-9,10-dihydroanthracenes suggests a boat conformation for the inside ring with the two outside rings in pseudoxial positions. The net effect of this geometry would be increased shielding of $H_{1'}H_{4'}H_{5'}H_{8'}$ but deshielding of H_4H_5 and $H_{4''}H_{5''}$. This latter effect is expected since these protons of the outside rings are in deshielding regions of each other in a dipseudoxial geometry. For the trans isomer, the central ring is expected to be nearly planar, resulting in increased shielding at $H_{1'}H_{4'}H_{5'}H_{8'}$. Moreover, since the outside rings are on opposite sides, the mutual deshielding is not present as with cis. We also note that the outside protons $H_1H_8H_{1''}H_{8''}$ move from a shielding region toward a deshielding region as the central ring is flattened. Hence the trans isomer should show different trends, as compared to cis, and protons $H_4H_5H_{4''}H_{5''}$ should exhibit an upfield shift and $H_1H_8H_{1''}H_{8''}$ downfield shift relative to dimer **8**. In fact, the NMR spectrum of the trimer shows an upfield shift for the $H_4H_5H_{4''}H_{5''}$ doublet of 0.1 to 0.15 ppm[22] relative to the dimer and a downfield shift for the $H_1H_8H_{1''}H_{8''}$ doublet of 0.2 ppm again relative to the dimer. Hence, the trimer structure is tentatively assigned as trans.

The fact that trimer is not observed in the reduction of ethyl anthroate does not preclude the possibility that eq 6 represents an important pathway for dimerization. The presence of two carbethoxy groups in the dimer/dianion depicted in eq 6 provides stabilization that is absent in the intermediate formed from anthracene dianion and ethyl anthroate. However, it is difficult to distinguish between this latter process (and related processes) and simple radical anion dimerization. Experiments designed to provide more insight were not conclusive (Table I). There is a concentration dependence with dimer formation increasing from 62% to 82% with a corresponding increase in ester concentration of 0.025 to 0.1 M. Moreover, slow

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(20) Results to be published. See also: Raber, D. J.; Hardee, L. E.; Rabideau, P. W.; Lipkowitz, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 2843.

(21) Fu, P. P.; Harvey, R. G.; Paschal, J. W.; Rabideau, P. W. *J. Am. Chem. Soc.* **1975**, *97*, 1145.

(22) The uncertainty is due to the fact that the central ring also shows a doublet here (H_1, H_4, H_5, H_8), and it is impossible to tell which of the partially overlapping doublets belongs to the outside rings (i.e., they are 0.05 ppm apart).

addition of the ester to a sodium/ammonia solution was carried out in an attempt to minimize radical anion concentration and increase dianion concentration early in the reaction (i.e., an effective large excess of metal early in the reaction). This did not produce a dramatic change, although a slight increase in monomer was observed. We conclude, therefore, that although radical anion dimerization may be the pathway for dimer formation under reduction conditions, we cannot completely rule out the other possibilities at this time.

Experimental Section

General Methods. Essentially all of the reductions described herein using the presence of water before metal addition produced product free of unreacted starting material or other contaminants (by NMR of the crude reaction product). The isolated yields in many cases involved the manipulation of relatively small amounts of materials and hence may not be representative of the maximum obtainable yields that should be excellent. NMR spectra were recorded on Varian EM-390 (proton) and CFT-20 (carbon) spectrometers with internal Me_4Si as reference. Notations in parentheses following carbon NMR data refer to multiplicities in off-resonance decoupled (or completely coupled) spectra.

General Methods for Metal–Ammonia Reductions.[18] The aromatic substrate along with 1.5 equiv of water was dissolved in 1 part THF (freshly distilled from benzophenone ketyl) and added to 2 parts of anhydrous ammonia, under inert gas, at −78 °C (or −33 °C). Sodium metal (1.25 equiv) was then added in pieces and the reaction was stirred for 25 min. The mixture was then poured (or pumped through a glass tube) into a large excess of NH_4Cl solution. Products were separated by ether partition.

Ethyl 1,4-Dihydrobenzoate.[23] Ethyl benzoate (7 g, 46 mmol) and water (69 mmol) were reacted with sodium (116 mmol) in 75 mL of THF/150 mL of NH_3 according to the general procedure. NMR indicated no other products. A colorless oil was obtained in 64% by vacuum distillation: bp 54–56 °C (0.35 mm); NMR (CCl_4) δ 5.8 (br s, 4 H), 4.1 (m, 2 H), 3.6 (m, 1 H), 2.7 (d, 2 H), 1.3 (t, 3 H).

***tert*-Butyl 1,4-Dihydrobenzoate.** *tert*-Butyl benzoate (1 g, 5 mmol) and water (8 mmol) were reacted with sodium (13 mmol) in 30 mL of THF/60 mL of NH_3 according to the general procedure. Microdistillation afforded a colorless oil, bp 54–55 °C (0.25 mm), in 40% yield: NMR (CCl_4) δ 5.7 (br s, 4 H), 3.5 (m, 1 H), 2.6 (m, 2 H), 1.4 (s, 9 H).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.33; H, 8.89; O, 17.78. Found: C, 72.96; H, 8.99.

***tert*-Butyl 1,4-Dihydronaphthoate.** *tert*-Butyl 1-naphthoate (1 g, 4 mmol) and water (6 mmol) were reacted with sodium (10 mmol) in 30 mL of THF/60 mL of NH_3, according to the general procedure. Microdistillation afforded a colorless oil, bp 192–194 °C (0.35 mm), in 42% yield: NMR (CCl_4) δ 7.1 (br s, 4 H), 5.9 (m, 2 H), 4.1 (m, 1 H), 3.3 (m, 2 H), 1.3 (s, 9 H).

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.26; H, 7.83; O, 13.91. Found: C, 78.03; H, 7.90.

***tert*-Butyl 1,4-Dihydro-*p*-toluate.** *tert*-Butyl *p*-toluate (1 g, 5 mmol) and water (8 mmol) were reacted with sodium (13 mmol) in 30 mL of THF/60 mL of NH_3 according to the general procedure. Microdistillation afforded a colorless oil, bp 32 °C (0.2 mm), in 37% yield.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.23; H, 9.28; O, 16.49. Found: C, 74.23; H, 9.28.

Ethyl 9,10-Dihydro-9-anthroate (7). 9-Ethyl anthroate (2.0 g, 8 mmol) and water (12 mmol) were reacted with sodium (20 mmol) in 50 mL of THF/100 mL of NH_3 at −33 °C according to the general procedure. An NMR spectrum of the crude material indicated 92% **7** and 8% dimer. Recrystallization from aqueous ethanol afforded **7** in 66% yield: mp 41–43 °C; ^1H NMR ($CDCl_3$) δ 7.21 (m, 8 H), 4.9 (s, 1 H; H_9), 4.3 ($^1/_2$ of AB pattern, 1 H; H_{10}), 3.95 (q, CH_2), 3.8 ($^1/_2$ of AB pattern, $H_{10'}$), 1.08 (t, 3H, CH_3) [signals at 4.3 and 3.8 overlap]; ^{13}C NMR ($CDCl_3$) δ 171.8 (s, C=O), 236.7 (s), 128.2, 128.0, 127.4, 126.4, 61.0 (t, -OCH_2-), 53.2 (d, C_9), 35.7 (t, C_{10}), 14.9 (q, CH_3).

Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39; O, 12.68. Found: C, 81.12; H, 6.54; O, 12.36.

***tert*-Butyl 9,10-Dihydro-9-anthroate (6).** *tert*-Butyl 9-anthroate (1.1 g, 4 mmol) was reduced as above to afford **6** in 65% yield after recrystallization from aqueous ethanol: mp 61–63 °C; ^1H NMR ($CDCl_3$) δ 7.21 (m, 8 H), 4.8 (s, 1 H, H_9), 4.05 (AB, 2 H, $H_{10}H_{10'}$), 1.28 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.0 (s, C=O), 136.5 (s), 134.3 (s), 128.1, 127.9, 127.2, 126.2, 81.1 (s, -$C(CH_3)_3$), 54.3 (d, C_9), 35.7 (t, C_{10}), 27.9 (t, CH_3).

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19; O, 11.41. Found: C, 81.52; H, 7.39; O, 11.33.

Reduction of Anthroate Esters under Anhydrous Conditions. A variety of conditions are described in Table I. Representative procedures for the preparation and isolation of dimeric products follow below.

Diethyl 9,9′,10,10′-Tetrahydro-9,9′-dianthroate (8). Sodium metal (5.1 mmol) was dissolved in 15 mL of THF/30 mL of NH_3 at reflux. Ethyl 9-anthroate (0.5 g, 2 mmol) was then added and stirring was continued for 30 min. The reaction mixture was then poured into 150 mL of aqueous NH_4Cl followed by the usual ether extraction. An NMR spectrum of the crude product indicated about 75% dimer. Isolation of pure **8**, mp 253–254 °C, was accomplished by recrystallization from a methanol/methylene chloride mixture in a 44% yield: ^1H NMR ($CDCl_3$) δ 7.45 (d, 4 H, $H_{1,1'}$, $H_{8,8'}$), 7.18 (t, 4 H, $H_{2,2'}$, $H_{7,7'}$), 6.89 (t, 4 H, $H_{3,3'}$, $H_{6,6'}$), 6.25 (d, 4 H, $H_{4,4'}$, $H_{5,5'}$), 5.05 (s, 2 H, $H_{9,9'}$), 4.23 (q, 4 H, CH_2), 4.08 (s, 2H, $H_{10,10'}$), 1.27 (t, 6 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 173.0 (s, C=O), 138.7 (s), 134.0 (s), 130.9, 129.2, 126.0, 61.7 (t, CH_2), 53.8 (d, C_{10}), 52.4 (d, C_9), 14.3 (q, CH_3); mass spectrum (chemical ionization; isobutane), MH^+, *m/e* 503 ($C_{34}H_{30}O_4$ = 502).

Anal. Calcd for $C_{34}H_{30}O_4$: C, 81.25; H, 6.02; O, 12.73. Found: C, 81.25; H, 6.18; O, 12.75.

Di-*tert*-butyl 9,9′,10,10′-Tetrahydro-9,9′-dianthroate. Reduction of *tert*-butyl 9-anthroate according to the procedure outlined immediately above gave the dimer in 36% yield: mp 332–334 °C dec; ^1H NMR ($CDCl_3$) δ 7.41 (d, 4 H, $H_{1,1'}$, $H_{8,8'}$), 7.14 (t, 4 H, $H_{2,2'}$, $H_{7,7'}$), 6.81 (t, 4 H, $H_{3,3'}$, $H_{6,6'}$), 6.21 (d, 4 H, $H_{4,4'}$, $H_{5,5'}$), 4.98 (s, 2 H, $H_{9,9'}$), 4.0 (s, 2 H, $H_{10,10'}$), 1.46 (s, 18H, CH_3); ^{13}C NMR ($CDCl_3$) δ 172.0 (s, C=O), 138.7 (s), 134.4 (s), 130.9, 129.4, 126.3, 125.8, 81.74 (s), 53.9 (d), 53.5 (d), 28.1 (q).

Anal. Calcd for $C_{38}H_{38}O_4$: C, 81.69; H, 6.85; O, 11.45. Found: C, 81.44; H, 6.88; O, 11.54.

Dimer 10. *n*-Butyllithium (1.1 equiv) was added to 9,10-dihydroanthracene (1.0 g) in THF (under N_2) at 0 °C. After being stirred for 30 min, the solution was pumped through a glass tube into a solution of ethyl anthroate (1 equiv) in NH_3/THF (3:1) at −33 °C. Stirring was continued for 20 min, and the reaction mixture was quenched with aqueous ammonium chloride and separated by ether extraction. HPLC analysis indicated 64% dimer **10**, 18% ethyl 9,10-dihydro-9-anthroate, 3% 9,10-dihydroanthracene, and 15% anthracene. Dimer **10** was crystallized from the mixture (ethanol): mp 214 °C; ^1H NMR ($CDCl_3$) δ 7.5–6.0 (16 H, aromatics, d, 7.4; d, 7.3; t, 7.1; t, 7.07; t, 6.83; t, 6.8; d, 6.3; d, 6.1), 5.1 (1, H_9), 4.35 (OCH_2), 4.15 (2, AB, $H_{10'a}H_{10'e}$), 3.95 (2, AB, $H_{10}H_{9'}$), 1.3 (3, t, CH_3); ^{13}C NMR ($CDCl_3$) δ 172.8 (C=O), 139.0 (s), 138.3 (s), 137.0 (s), 133.7 (s), 130.4, 130.1, 129.2, 127.2, 126.3, 126.1, 126.0, 125.3, 61.7 (t, OCH_2), 55.1 (d, $C_{9'}$), 52.3 (d, C_9), 50.6 (d, C_{10}), 35.9 (t, $C_{10'}$), 14.3 (q, CH_3).

Anal. Calcd for $C_{31}H_{26}O_2$: C, 86.47; H, 6.10; O, 7.43. Found: C, 86.22; H, 6.21.

Trimer 12. Anthracene dianion was prepared by reaction of 0.5 g of 9,10-dihydroanthracene in 10 mL of THF at 0 °C with 2 equiv of *n*-butyllithium. Stirring was continued for 20 min, and the solution was then added through a double-tipped needle to 1 equiv of ethyl 9-anthroate in THF (15 mL)/NH_3 (50 mL) at −33 °C. After continued stirring, this mixture was pumped into aqueous ammonium chloride and then extracted with ether. As reported above, this product was then analyzed (see text) by reverse-phase HPLC on a RCM C-18 column with acetonitrile/water (70:30). Extracting the ether extract product with boiling 95% ethanol dissolved everything except the trimer and some anthracene. this residue was ground up and extracted again with hot 95% ethanol and then recrystallized from ethyl acetate to provide pure trimer: mp 245 °C; ^1H NMR ($CDCl_3$), aromatic H's

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[23] Plieninger, H.; Ege, G.; Jung, F.; Maier-Borst, W. *Chem. Ber.* **1961**, *94*, 2088.

at δ 7.65 (d), 7.35 (t), 7.15 (t), 6.77 (m) and 6.12 (m) totalling 24 H's; δ 5.2 (s, 2 H), 4.25 (q, 4 H; CH_2CH_3), 4.26 (AB, J = 10.5 Hz, 4 H), 1.2 (t, 6 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 172.5 (s, C=O), 139 (s), 138.3 (s), 134.3 (s), 131.1, 130.9, 130.0, 126.7, 126.1, 124.8, 61.8 (t), 55.8 (d), 53.8 (d), 52.6 (d), 14.2 (q).

Anal. Calcd for $C_{48}H_{40}O_4$: C, 84.71; H, 5.88; O, 9.41. Found: C, 84.68; H, 6.01.

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Registry No. **5**, 89302-36-3; **6**, 89302-39-6; **7**, 89302-38-5; **8**, 89302-40-9; **10**, 89302-42-1; **12**, 89302-43-2; Na, 7440-23-5; Li, 7439-93-2; K, 7440-09-7; di-*tert*-butyl 9,9',10,10'-tetrahydro-9,9'-dianthroate, 89302-41-0; ethyl 1,4-dihydrobenzoate, 29246-24-0; *tert*-butyl 1,4-dihydrobenzoate, 61812-52-0; *tert*-butyl 1,4-dihydro-*p*-toluate, 89302-37-4; ethyl benzoate, 93-89-0; *tert*-butyl benzoate, 774-65-2; *tert*-butyl naphthoate, 66821-79-2; *tert*-butyl *p*-toluate, 13756-42-8; ethyl 9-anthroate, 1754-54-7; *tert*-butyl 9-anthroate, 1734-16-3; 9,10-dihydroanthracene, 613-31-0.

Rivularins. Preliminary Synthetic Studies

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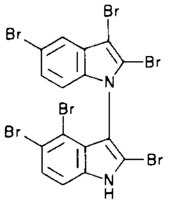
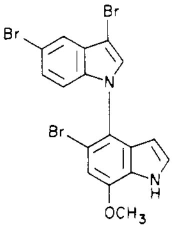
The 3,4'-biindole system of rivularin D has been synthesized from 1-(2,2-dimethoxyethyl)-2-methyl-3-nitrobenzene by consecutive Batcho–Leimgruber and Fischer indolizations. 5-Bromo-3-(2-methyl-3-nitrophenyl)-1*H*-indole could be converted to 5-bromo-1-methyl-3,4'-bi-1*H*-indole or 10-bromo-7-methyl-7*H*-naphth[2,1-*b*]indol-4-amine by heating with *N*,*N'*-dimethylformamide dialkyl acetal, followed by reduction with Raney nickel/hydrazine. In contrast to the generally operative alkylation mechanism which involves the alkoxy groups of the intermediate alkoxyimminium ion derived from the *N*,*N*-dialkylformamide dialkyl acetal, the N-methylation reactions presented here are shown to be unique examples where the N-methylation step is effected by the *N*-methyl groups of *N*,*N*-dimethylformamide dimethyl acetal.

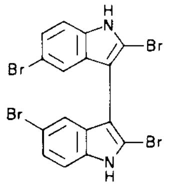
A number of brominated biindoles that exhibit a variety of nuclear connectivities and substitution patterns unprecedented among known naturally occurring biindoles were recently isolated from the blue-green alga *Rivularia firma* Womersley.[1] The size and location of the substituents generate atropisomerism, rendering most of these compounds optically active. Intended to suggest the source (Rivularia) and the chemical character (indole), the proposed generic term "rivularin" is a cumulative description of this class of compounds. The added letters A, B, C, and D represent 1–3', 1–4', 3–3', and 3–4' intramolecular linkages, respectively, between the indole nuclei.



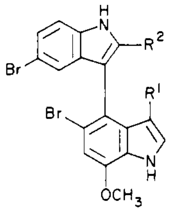
1
Rivularin A



2
Rivularin B



3
Rivularin C



4a: R^1 = Br, R^2 = H; Rivularin D_1

4b: R^1 = H, R^2 = Br; Rivularin D_2

4c: R^1 = R^2 = Br; Rivularin D_3

Of these biindoles, rivularin D_3 (**4c**) was of synthetic interest to us in view of its antiinflammatory activity. Our plan, therefore, consisted of the development of a reaction sequence that would first lead to the molecular rivularin D skeleton but also permit the synthesis of the 5,5'-dibromo-7-methoxy derivative from corresponding functionalized benzenoid precursors. The remaining two bromine substituents at the indole positions 2' and 3 would then have to be introduced in the final steps of the synthesis leading to racemic rivularin D_3.

The anticipated routes toward the monobrominated rivularin D nucleus (**7**), as outlined in Scheme I, were partial to the use of the two starting materials **5** and **10**, whose synthesis we had described recently.[2] Sequence A commences with a Fischer indolization of the enol ether **5**; the second indole would then be constructed by a Batcho–Leimgruber reaction from the resulting 5-bromo-3-(2-methyl-3-nitrophenyl)-1*H*-indole (**6**). The basic strategy in sequence B consists of the order reversal of the two indolizations.

In accordance with sequence A, **6** was prepared in acceptable yields, but the subsequent reaction with *N*,*N*-dimethylformamide dimethyl acetal proceeded with some unexpected results, which are summarized in Scheme II. Refluxing **6** in a mixture of *N*,*N*-dimethylformamide dimethyl acetal and *N*,*N*-dimethylformamide, followed by reductive cyclization of the resulting enamine, indeed gave rise to the expected biindole system, but the product (**8**) was N-methylated. Mass spectrometric proof for the N-methylation site in **8** was unavailable, since losses of bromine and methyl preceded further fragmentations, but the ^1H NMR spectrum revealed a singlet for H2 in one and a doublet of doublets for both H2 and H3 in the other indole moiety so that the structure of **8** was established.

Hoping to prevent the N-methylation step during the Batcho–Leimgruber sequence, we prepared the *N*-acetyl,

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(1) Norton, R. S.; Wells, R. J. *J. Am. Chem. Soc.* **1982**, *104*, 3628.

(2) Maehr, H.; Smallheer, J. *J. Org. Chem.* **1981**, *46*, 1752.