Metal–Ammonia Reduction. VI. Stereospecific Alkylation of the 9-Alkyl-9,10-dihydro-10-anthryl Carbanion[1,2]

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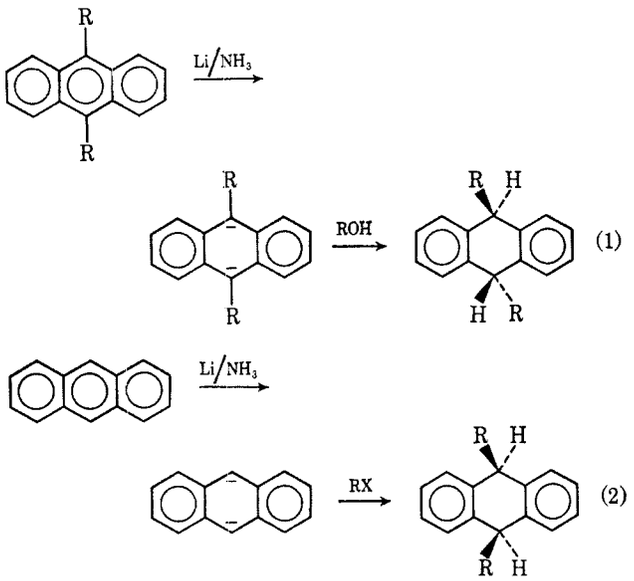
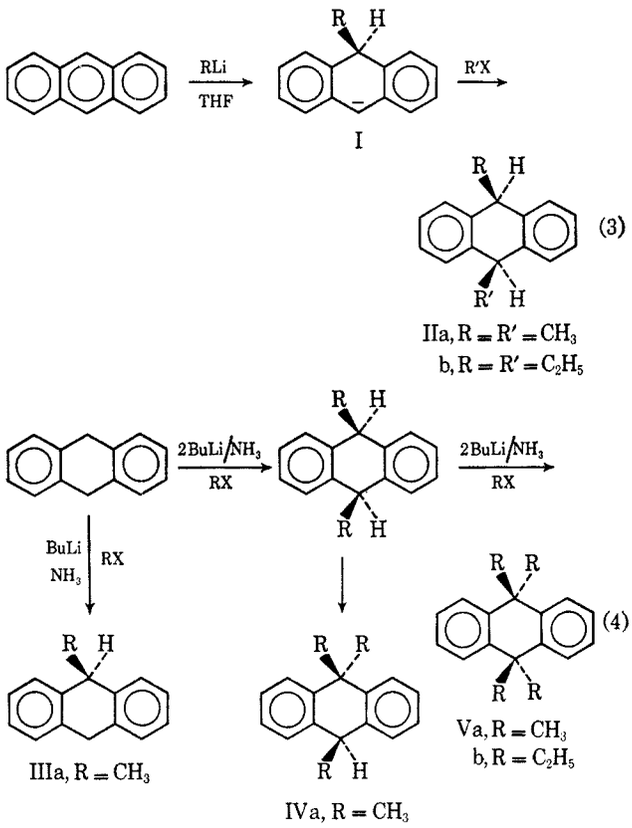
cis-9,10-Dialkyl-9,10-dihydroanthracenes are synthesized stereospecifically by addition of an alkyllithium reagent to anthracene in tetrahydrofuran and alkylation with an alkyl halide (method A) or alkylation of 9,10-dihydroanthracene with *n*-butyllithium in ether–ammonia and excess alkyl halide (method B). Analogous reactions in the benz[*a*]anthracene and dibenz[*a,h*]anthracene series proceed with similar stereospecificity.

Stereospecific *trans* reduction[3] of 9,10-dialkylanthracene by lithium in liquid ammonia (eq 1) and stereospecific *cis*-reductive alkylation[2] of anthracene in the same medium (eq 2) have recently been reported.



The scope of reductive alkylation is limited by the required identity of the alkyl groups introduced, by the markedly lower yields and more complex product mixture from reaction on larger (>10 mmol) scale, and by the secondary formation of 9,9,10-trialkyl-9,10-dihydroanthracene (approximately 20% under optimum conditions). We now wish to report two related and complementary stereospecific synthesis of the *cis*-9,10-dialkyl-9,10-dihydroanthracenes (II) largely free of these limitations.

In the first method (A), the 9-alkyl-9,10-dihydro-10-anthryl carbanion (I) was prepared *via* addition of an alkyllithium reagent to anthracene in tetrahydrofuran[4] and alkylated *in situ* with excess alkyl halide[5] (eq 3). In the second method (B), 9,10-dihydroanthracene dissolved in ether–ammonia (at −33°) was treated in sequence with *n*-butyllithium and excess alkyl halide to provide 9-alkyl-9,10-dihydroanthracene (III) or II as the major product, depending upon the proportion of the reagents employed (eq 4). Repetition of the latter sequence on II provided the corresponding 9,9,10-trialkyl- and 9,9,10,10-tetraalkyl-9,10-dihydroanthracenes (IV and V). In principle, any combination of alkyl groups may be introduced in these operations.



In a typical addition–alkylation (eq 3) experiment, ethyllithium (2 equiv) in benzene was added to a solution of anthracene in tetrahydrofuran at 0°. The red color of the resulting carbanion (I) was discharged after 40 min by the addition of ethyl bromide. Glpc analysis[6] revealed IIb (95%) as the major product.

Analogous transformations employing ethyl-, isopropyl-, *n*-butyl-, and *t*-butyllithium reagents in combination with methyl, ethyl, *n*-butyl, and isopropyl halides proceeded with similar facility and stereospecificity (Table I). The stereochemical assignments of IIa and IIb are based upon chemical and spectral evidence presented in detail in preceding papers;[2,3] *cis* geometry is assumed for the remaining members of the series on the basis of analogy. Although methyl-

(1) This investigation was supported in part by Public Health Grant CA-08674 from the National Cancer Institute. Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968.

(2) Part V: R. G. Harvey and L. Arzadon, *Tetrahedron*, in press.

(3) R. G. Harvey, L. Arzadon, J. Grant, and K. Urberg, *J. Amer. Chem. Soc.*, **91**, 4535 (1969).

(4) D. Nicholls and M. Szwarc, *ibid.*, **88**, 5757 (1966); *Proc. Roy. Soc.*, **A301**, 231 (1967).

(5) Synthesis of the 9,10-diethyl, di-*n*-butyl, and dibenzyl analogs of II *via* method B was cited without experimental detail in paper IV.[3]

(6) A 6-ft column of 10% SE-30 on Chromosorb W at 150° was employed.

TABLE I

cis-9,10-DIALKYL-9,10-DIHYDROANTHRACENES (II)

R	R′	Method	Yield, %	Mp, °C	Calcd, % C	Calcd, % H	Found, % C	Found, % H
C_2H_5	CH_3	A	95	103.2–103.6[a]				
i-C_3H_7	CH_3	A	70	65.5–66.5	91.47	8.53	91.62	8.50
n-C_4H_9	CH_3	A	85	61.0–61.6	91.14	8.86	91.09	8.74
t-C_4H_9	CH_3	A	63	115.5–117	91.14	8.86	91.10	8.69
C_2H_5	C_2H_5	A (B)	95 (86)	58–59[b]	91.45	8.53	91.07	8.76
i-C_3H_7	*i*-C_3H_7	A	80	74–74.5[b]				
n-C_4H_9	*n*-C_4H_9	A (B)	92 (74)	Oil	90.35	9.65	90.45	9.59
CH_3	CH_3	B	69	130–131[b]				
$C_6H_5CH_2$	$C_6H_5CH_2$	B	90	111–112.5[c]	93.29	6.71	93.09	6.76

[a] Reference 2. [b] Reference 3. [c] A 9,10-dibenzyl-9,10-dihydroanthracene (mp 119°) of unknown stereochemistry was reportedly[12] obtained on reduction of 9,10-dibenzylanthracene with sodium in pentyl alcohol.

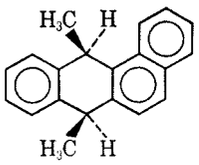
lithium failed to enter into reaction with anthracene[7] at 0°, adduct formation and alkylation occurred at 50° to afford approximately equal amounts of *cis* and *trans* isomers of IIa (56%). Analogous addition of organolithium reagents to naphthalene, reported by Eppley and Dixon,[9] requires still more vigorous conditions.

The choice of solvent proved important. Thus, reaction between *n*-butyllithium and anthracene, as determined through glpc analysis of the products of ethanolysis, proceeded to virtual completion in tetrahydrofuran or triethylamine, and not at all in petroleum ether or benzene. This difference may relate to the varying extent of aggregation of the organolithium reagent in these media (*e.g.*, *n*-butyllithium is hexameric in benzene and tetrameric in tetrahydrofuran[8,10] at 25°). In tetrahydrofuran, the solvent adopted for general usage, slightly more than 2 equiv of the organolithium reagent were required for maximum yield. To some extent, this excess is necessary to compensate for partial loss due to attack on the solvent.[11]

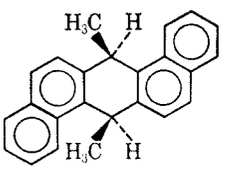
Method B (eq 4), has precedent in that analogous reactions in ether have been reported.[12] However, substitution of ammonia–ether for ether alone has been found generally, and sometimes dramatically, to improve the yields while diminishing formation of secondary products. For example, parallel ethylations of dihydroanthracene with *n*-butyllithium[13] and ethyl bromide furnished IIb (85%), IIIb (5%), and IVb (9%) in ammonia–ether and IIb (49%), IIIb (17%), IVb (12%), Vb (9%), and anthracene (10%) in ether alone. Analogous methylation provided IIa (70%), IIIa (3%), IVa (20%), and Va (7%) in ammonia–ether and six products (of which IIa and the corresponding *trans* isomer together accounted for 27% of the total) in ether alone. This solvent effect is undoubtedly related to the ability of anthracene to form a stable dianion in liquid ammonia,[14] whereas a radical anion is favored in ether and other less polar media.[15]

It is pertinent to inquire whether monoanion formation achieves completion before abstraction of the second proton begins. Affirmative evidence was provided by a methylation experiment conducted in the presence of only 1 equiv of *n*-butyllithium; the sole product, according to glpc analysis,[6] was IIIb. Transformation beyond the dialkylated stage requires proton abstraction from II or III followed by further alkylation a process unlikely to compete effectively with direct alkylation of excess alkyllithium reagent. In agreement with this expectation, the yield of IIa remains approximately 70%, whether 2, 3, or 4 equiv of *n*-butyllithium are employed.

Compounds synthesized by method B include, in addition to the 9-monoalkyl (IIIa and IIIb) and 9,10-dialkyl (IIa and IIb; also II, R = *n*-C_4H_9, $C_6H_5CH_2$) derivatives of dihydroanthracene, the related *cis*-dimethyl derivatives of 7,12-dihydrobenz[*a*]anthracene (VI) and 7,14-dihydrodibenz[*a*,*h*]anthracene (VII). Also, the trimethyl and tetramethyl compounds IVa and Va were conveniently synthesized by analogous monomethylation and dimethylation, respectively, of IIa.



VI



VII

Experimental Section

Materials and Methods.—All solvents were distilled from and dried over CaH_2. Liquid ammonia was distilled into the reaction vessel through a column of barium oxide.[16] Organolithium reagents were used as supplied by the Foote Mineral Co. Anthracene and 9,10-dihydroanthracene (Aldrich) were recrystallized from alcohol and dried *in vacuo*. 7,12-Dihydrobenz[*a*]anthracene and 7,14-dihydrodibenz[*a*,*h*]anthracene were prepared by lithium–ammonia reduction of benz[*a*]anthracene[17] and dibenz[*a*,*h*]anthracene,[3] respectively. The alkyl halides employed, with the exception of isopropyl chloride and benzyl chloride, were bromides; all were purified before use either by distillation or, in the case of methyl bromide, passage through a column of activated silica gel.

Proton nmr spectra were obtained on a Varian A-60 spectrometer with chemical shifts reported relative to tetramethylsilane

(7) The low reactivity of methyllithium is presumably a consequence of its relatively low nucleophilicity relative to other alkyllithium reagents and its strong tendency to aggregation in solution (it is tetrameric even in tetrahydrofuran[8]).

(8) T. L. Brown, *Accounts Chem. Res.*, **1**, 23 (1968).

(9) R. L. Eppley and J. A. Dixon, *J. Amer. Chem. Soc.*, **90**, 1606 (1968).

(10) P. West and R. Waack, *ibid.*, **89**, 4395 (1967).

(11) H. Gilman and B. J. Gaj, *J. Org. Chem.*, **22**, 1165 (1957); H. Gilman and S. Gray, *ibid.*, **23**, 1476 (1958); H. Gilman and G. L. Schwebke, *J. Organometal. Chem.*, **4**, 483 (1965).

(12) A. L. J. Beckwith and W. A. Waters, *J. Chem. Soc.*, 1001 (1957).

(13) A 25% excess over that required for dianion formation was employed. Products were identified by retention times on the glpc column[6] by comparison with those of the authentic compounds.

(14) H. Smith, "Organic Reactions in Liquid Ammonia," Vol. 1, Part 2, John Wiley & Sons, Inc., New York, N. Y., 1963.

(15) D. E. Paul, D. L. Lipkin, and S. I. Weissman, *J. Amer. Chem. Soc.*, **78**, 116 (1956).

(16) R. G. Harvey, *J. Org. Chem.*, **32**, 238 (1967).

(17) R. G. Harvey and K. Urberg, *ibid.*, **33**, 2206 (1968).

in deuteriochloroform. All reactions were carried out under nitrogen in dry glassware. Microanalyses were performed by Microtech Laboratories, Skokie, Ill.

Addition–Alkylation.—In a typical experiment, ethyllithium (54 mmol) in benzene was added to a solution of anthracene (25 mmol) in tetrahydrofuran (125 ml) at 0°, and the resulting deep red color was discharged after 40 min by the addition of excess ethyl bromide. The product was partitioned between ether and water, dried over $MgSO_4$, and evaporated to provide crude IIb (95% by glpc[6]). Recrystallization from ethanol provided the analytical sample (Table I).

Alkylation of 9,10-Dihydroanthracene.—To a refluxing solution of 9,10-dihydroanthracene (3.6 g, 20 mmol) in ether (75 ml) and liquid ammonia (150 ml) in a Morton flask was added 31.3 ml of a 1.6 *M* solution of *n*-butyllithium (50 mmol) in hexane. The resulting dark red solution was stirred for 1 hr, then decolorized by the addition of ethyl bromide. Water (10 ml) was added, and the ammonia was allowed to evaporate. Work-up by extraction with ether provided crude IIb (86% by glpc[6]); the nmr spectrum of a recrystallized sample matched that of previously prepared IIb. Two other components of the crude product were characterized as IIIb (5%) and IVb (9%) by comparison of glpc retention times and nmr spectra with those of the authentic substances.

All other alkylations were carried out by essentially the same procedure.

II (R = R′ = $C_6H_5CH_2$) proved exceptional in that it underwent decomposition on the glpc column (4-ft 2% Apiezon L) at 125° to furnish anthracene and bibenzyl. The latter were identified by glpc retention times and nmr spectra of samples trapped off the glpc column.

9,9,10-Trimethyl-9,10-dihydroanthracene (IVa).—Analogous methylation of IIa (10 mmol) in ether–ammonia with *n*-butyllithium (16 mmol) and excess methyl bromide afforded a white solid (2.17 g) consisting of IVa (90%) and IIa (9%) by glpc.[6] Recrystallization from ethanol provided IVa melting at 81–82.5°.

Anal. Calcd for $C_{17}H_{18}$: C, 91.84; H, 8.16. Found: C, 91.57; H, 8.20.

***cis*-7,12-Dimethyl-7,12-dihydrobenz[*a*]anthracene (VI).**—Except for the use of tetrahydrofuran in place of ether, analogous conditions were employed for the methylation of 7,12-dihydrobenz[*a*]anthracene (5 g). The crude product, a viscous oil, crystallized upon chromatography on a column of neutral alumina. Recrystallization from ethanol provided VI, 2.24 g, mp 103.5–105° (lit.[2] mp 106–107°).

***cis*-7,14-Dimethyl-7,14-dihydrodibenz[*a*,*h*]anthracene (VII).**—Methylation of 7,14-dihydrodibenz[*a*,*h*]anthracene in tetrahydrofuran–ammonia provided crude VII (isolated by extraction with ethyl acetate) in apparently quantitative yield (according to glpc on a 6-ft 1.5% OV-1 column at 250°). Recrystallization from ethyl acetate provided VII melting at 215–216.5° (lit.[2] mp 215–216.5°).

Nmr spectra.—All assigned structures were confirmed by nmr spectroscopy. The following summary of nmr data includes only compounds whose nmr spectra have not been previously reported.[2,3]

II (**R** = *i*-C_3H_7; **R′** = CH_3) showed 432 (m, 8, aryl), 244 (q, 1, $CHCH_3$, J = 7 Hz), 210 [d, 1, $CHCH(CH_3)_2$, J = 7 Hz], 95 (d, 3, CH_3, J = 7 Hz), and 55 cps (d, 6, CH_3, J = 7 Hz); the remaining methine proton appeared as a broad, weak band.

II (**R** = *n*-C_4H_9; **R′** = CH_3) showed 432 (m, 8, aryl), 243 (q, 1, $CHCH_3$, J = 7 Hz), 231 (t, 1, $CHCH_2$, J = 7.5 Hz), and 93 cps (d, 3, CH_3CH, J = 7.5 Hz); the remaining protons appear as a broad band in the aliphatic region.

II (**R** = *t*-C_4H_9; **R′** = CH_3) showed 440 (m, 8, aryl), 245 (q, 1, $CHCH_3$, J = 6.5 Hz), 224 (s, 1, CH), 104 (d, 3, CH_3CH, J = 6.5 Hz), and 55 cps (s, 9, CH_3).

II (**R** = **R′** = *n*-C_4H_9) showed 432 (m, 8, aryl) and 230 cps (t, 2, CH, J = 7 Hz); the remaining bands overlap.

II (**R** = **R′** = $C_6H_5CH_2$) showed 435 and 425 (m, 18, aryl), 253 (t, 2, CH, J = 7 Hz), and 179 cps (d, 4, CH_2, J = 7 Hz).

IVa showed 450 (m, 2, aryl), 436 (m, 6, aryl), 248 (q, 1, CH, J = 7 Hz), 105 (s, 3, CH_3), 95 (s, 3, CH_3), and 90 cps (d, 3, CH_3, J = 7 Hz).

Registry No.—II (R = *i*-C_3H_7; R′ = CH_3), 21438-93-7; II (R = *n*-C_4H_9; R′ = CH_3), 21438-94-8; II (R = *t*-C_4H_9; R′ = CH_3), 21438-95-9; II (R = *n*-C_4H_9; R′ = *n*-C_4H_9), 21438-96-0; II (R = $C_6H_5CH_2$; R′ = $C_6H_5CH_2$), 21438-97-1; IVa, 14923-29-6.

Formation of Tri-*t*-butyl Orthoformate and *t*-Butyl Di-*t*-butoxyacetate in the Reactions of Chlorodifluoromethane and Dichlorofluoromethane with Potassium *t*-Butoxide[1]

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The reaction of dichlorofluoromethane with potassium *t*-butoxide in *t*-butyl alcohol solution yields a mixture of *cis*- and *trans*-1,2-di-*t*-butoxy-1,2-difluoroethylene and tri-*t*-butyl orthoformate. Chlorodifluoromethane yields the same products plus *t*-butyl difluoromethyl ether. In either case, if the reaction mixture is allowed to become acidic, *t*-butyl di-*t*-butoxyacetate may be formed, by solvolysis of the di-*t*-butoxydifluoroethylenes. The reactions are believed to be initiated by the formation of dihalomethylenes, which are transformed to *t*-butoxyfluoromethylene, from which the ortho ester and the dialkoxydifluoroethylenes are formed.

Cleaver has reported that the reaction of chlorodifluoromethane (not dichlorodifluoromethane, as stated in *Chemical Abstracts*) with the potassium salts of several secondary and tertiary alcohols yields 1,2-dialkoxy-1,2-difluoroethylenes and, in cases where secondary alkoxides are used, trialkyl orthoformates.[2]

$$CHClF_2 + ROK \longrightarrow ROCF{=}CFOR$$

Potassium *t*-butoxide gave a mixture of *cis* and *trans* isomers in about 25% yield, with no other products being noted. Potassium isopropoxide gave a smaller but unstated yield of 1,2-difluoro-1,2-diisopropoxyethylenes with the only other observed product being triisopropyl orthoformate. The difluorodialkoxyethylenes may be formed by the dimerization of intermediate alkoxyfluoromethylenes.[3] If so, they should also be formed, perhaps in higher yield, from dichlorofluoromethane, whose reaction with alkali-metal alkoxides passes almost entirely through the alkoxyfluoromethy-

(1) Part XXVII in the series "Methylene Derivatives as Intermediates in Polar Reactions." For part XXVI, see J. Hine, R. B. Duke, and E. F. Glod, *J. Amer. Chem. Soc.*, **91**, 2316 (1969). This work was supported in part by National Science Foundation Grants GP-2002, GP-4445, and GP-7629.

(2) C. S. Cleaver, U. S. Patent 2,853,531 (1958); *Chem. Abstr.*, **53**, 5135*f* (1959).

(3) J. Hine, "Divalent Carbon," The Ronald Press Co., New York, N. Y., 1964, p 68.