A Novel Synthesis of 2-Naphthols, Phenanthrols, Anthracenes, and Other Polycyclic Aromatic Products

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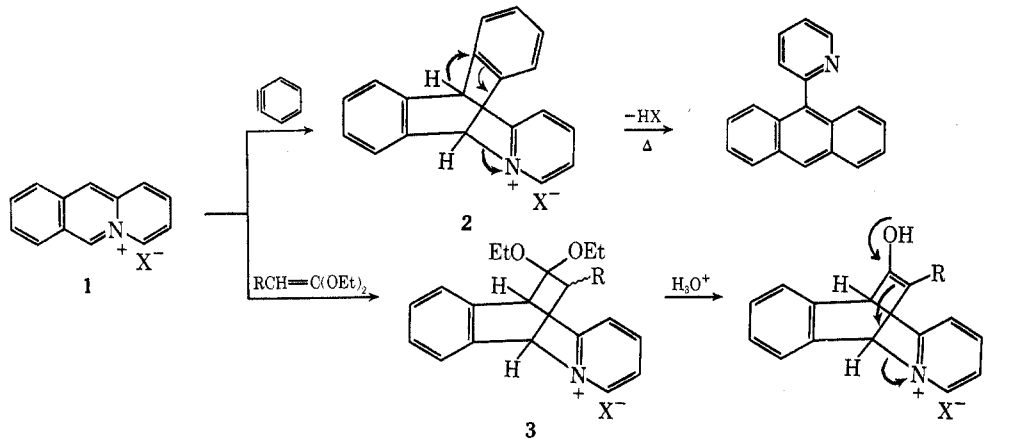
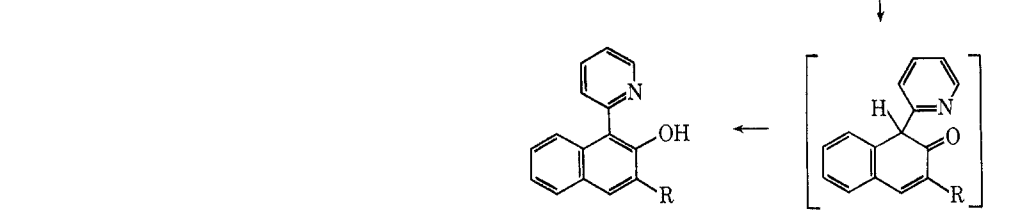
A simple and convenient synthesis of a number of new, or difficultly accessible, substituted 2-naphthols, phenanthrols, and related compounds is described, consisting of catalytic or chemical reduction of the appropriate ketene acetal–azoniapolycyclic adduct followed by a retrograde Diels–Alder reaction, which occurs upon heating of the reduction product in the presence of 6 *N* hydrochloric acid. Several substituted anthracenes and pentaphene were prepared similarly by sequential reduction and thermolysis of benzyne adducts of 4a-azoniaanthracene perchlorates and of 4a,8a-diazoniapentaphene diperchlorate, respectively. The scope and limitations of these syntheses are discussed.

In several of our recent publications we have dealt with the syntheses and properties of novel compounds derived from 4 + 2 cycloadducts of various azoniapolycyclic aromatic compounds with benzyne[1] and with ketene acetals.[2] The thermolysis of benzyne adducts such as **2**[1] and the hydrolysis followed by thermolysis of ketene acetal adducts such as **3** were shown to give (2-pyridyl)-substituted aromatic products according to eq 1 and 2, respectively.



(1)



(2)

If the pyridinium moiety of either of these two types of adducts is reduced prior to the hydrolysis and/or thermolysis steps, an alternate course of reaction will become available, specifically, a retrograde Diels–Alder reaction, which ultimately yields the same parent hydrocarbons as above, minus the pyridyl substituent (eq 3 and 4).

In this paper we report the results of our investigation of the applicability of these two reaction sequences as new general methods for preparing the title compounds. We have found that these syntheses do show considerable promise for providing research quantities of a variety of substituted 2-naphthols, anthracenes, etc., which are difficult to prepare, if not inaccessible, by other routes now known.

Naphthols and Phenanthrols—As a way of elaborating on the scope of these syntheses, we shall first consider details relevant to the step-by-step construction of a multisubstituted 2-naphthol, **4** (Scheme I). Azoniaanthracene salts (**1**) generally are prepared in good to excellent yields by allowing a 2-formyl-[3] [or preferably 2-(1,3-dioxolan-2-yl)-],[4] 2-acetyl-,[5] or 2-benzoylpyridine[5] to react with the appropriate benzyl halide, the resulting quaternary salt being cyclodehydrated by acid treatment. Although R_1 in azoniaanthracenes thus far described has been limited to H, CH_3, and C_6H_5, the availability of a variety of types of substituted benzyl halides gives one considerable latitude in the choice of R_5–R_8 substituents.

The R_3 substituent is established through selection of the ketene acetal to be used in preparing the inter-

(1) D. L. Fields, T. H. Regan, and R. E. Graves, *J. Org. Chem.*, **36**, 2995 (1971).

(2) (a) D. L. Fields, T. H. Regan, and J. C. Dignan, *ibid.*, **33**, 390 (1968); (b) D. L. Fields and T. H. Regan, *ibid.*, **35**, 1870 (1970); (c) **36**, 2986 (1971); (d) **36**, 2991 (1971).

(3) C. K. Bradsher and L. E. Beavers, *J. Amer. Chem. Soc.*, **77**, 4812 (1955).

(4) C. K. Bradsher and J. C. Parham, *J. Org. Chem.*, **28**, 83 (1963).

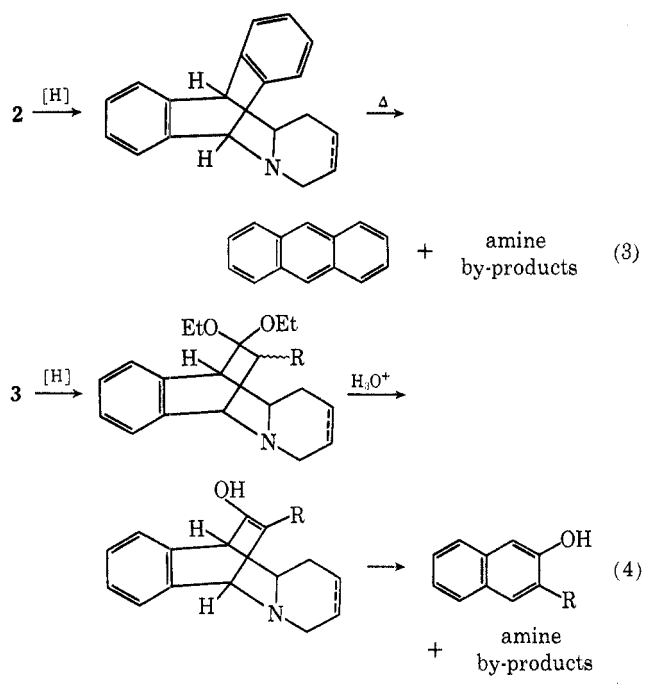
(5) C. K. Bradsher and T. W. G. Solomons, *J. Amer. Chem. Soc.*, **81**, 2550 (1959).

TABLE I

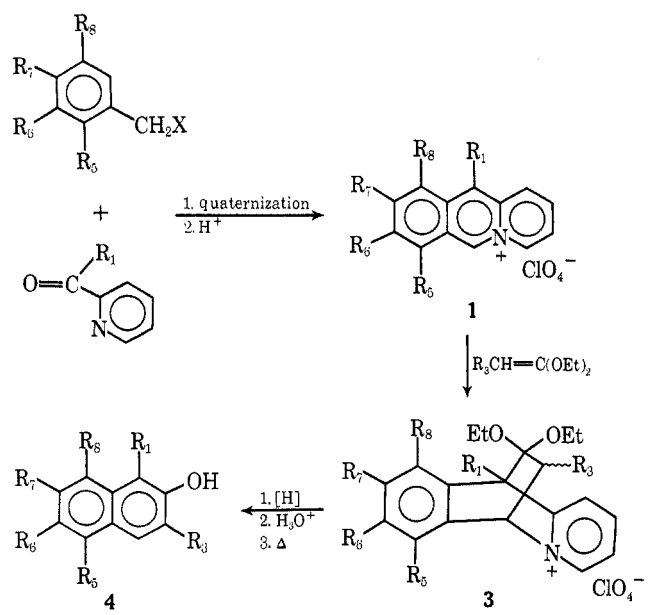
NAPHTHALENES PREPARED FROM KETENE ACETAL-AZONIAANTHRACENE ADDUCTS

Precursor	Product	Mp, °C	Yield, %	Calcd, % C	Calcd, % H	Found, % C	Found, % H
3a[a]	2-Naphthol		83				
3b[b]	1-Phenyl-2-naphthol[c]		71				
3c[a]	3-Methyl-2-naphthol[d]		96				
3d[a]	3-Phenyl-2-naphthol	117–118	92	87.3	5.5	87.3	5.7
3e[a]	3-Bromo-2-naphthol[e]		45				
3f[b]	3,5-Dimethyl-2-naphthol	126–127	83	83.7	7.0	83.5	7.3
3g[b]	3,5,8-Trimethyl-2-naphthol	126–127	90	83.9	7.5	84.3	7.7
3h[b]	5-Nitro-2-naphthol[f]		91				
3i[b]	7-Methyl-2-naphthol[g]		89				
3j[h]	1,6-Diacetoxy-4-*tert*-butylnaphthalene	101–103	47	72.0	6.7	71.6	7.1
3k[h]	1,2,6-Triacetoxy-4-phenylnaphthalene	137–143	54	69.8	4.8	69.8	5.1

[a] Reference 2a. [b] New adduct. See Experimental Section. [c] W. Henderson and E. Ullman, *J. Amer. Chem. Soc.*, **87**, 5424 (1965). [d] J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 817 (1937). [e] C. Marschalk, *Bull Soc. Chim. Fr.*, **43**, 1361 (1928). [f] A. Cohen, J. W. Cook, C. L. Hewett, and A. Girard, *J. Chem. Soc.*, 653 (1934). [g] Reference 8. [h] Reference 2c.



SCHEME I



mediary cycloadduct **3**. The experimental details related to cycloaddition reactions of ketene acetals to azoniaanthracene salts have been adequately described in earlier papers,[2] and it will suffice to say that such additions generally occur rapidly and regiospecifically,[6] and provide good to quantitative yields of adduct.

The reduction of the pyridinium moiety in the next step is accomplished by either catalytic or chemical means. Hydrogenation of adducts to give piperidino products has been effected in a Parr hydrogenation apparatus using H_2 at 60 psi over PtO_2. Alternatively, pyridinium ring reduction can be achieved within minutes by employing excess sodium borohydride in methanolic sodium methoxide solution. Whether the pyridinium ring is completely or only partly reduced apparently is unimportant.

Except for the more acid-sensitive products,[7] the final two steps, hydrolysis of the ketal and thermolysis, can be conducted simultaneously by simply heating the reduction product in refluxing 6 *N* hydrochloric acid. These steps are conveniently carried out in a two-phase system consisting of 6 *N* hydrochloric acid and an organic solvent such as toluene, so that the naphthol formed during the thermolysis is extracted into the toluene, effectively separating it from the amine hydrochloride by-product which remains in the aqueous phase. After 0.5–1-hr reflux, the toluene layer is separated and concentrated, yielding the naphthol in a good state of purity.

In Table I are listed 2-naphthols that have been prepared by this procedure and in Table II are shown the products derived from ketene acetal adducts of more complex starting azoniapolycyclics. The reported yields are based on single experiments run on a 1–10-g scale. The structural assignments for all new products were supported by elemental analysis and the usual (uv, ir, nmr) spectral means.

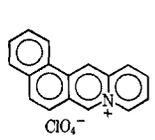
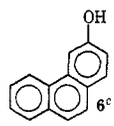
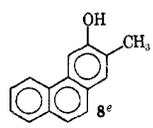
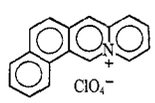
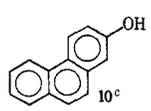
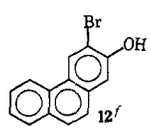
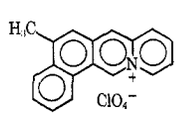
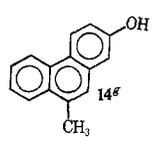
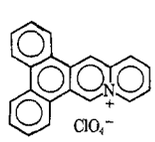
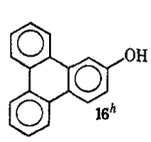
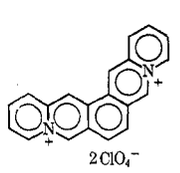
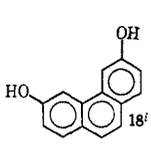
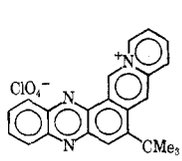
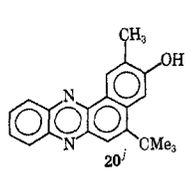
Anthracenes.—In light of the previous discussions, the synthesis of anthracenes *via* adducts of benzyne and substituted 4a-azoniaanthracenes, *i.e.*, 4a-azoniatriptycenes (eq 3), is straightforward and needs little clarification. Anthracenes that we have prepared by

(6) A. Hassner, *J. Org. Chem.*, **33**, 2684 (1968).

(7) For example, 8-*tert*-butylnaphthalenes are prone to de-*tert*-butylate in the presence of strong acid, especially at elevated temperatures. Therefore, in the synthesis of 1,6-diacetoxy-4-*tert*-butylnaphthalene, Table I, the ketal hydrolysis step was carried out at room temperature, and the resulting ketone was isolated and then thermolyzed in acetic anhydride–sodium acetate at reflux temperature. 1,2,6-Triacetoxy-4-phenylnaphthalene was prepared similarly.

TABLE II

PRODUCTS DERIVED FROM VARIOUS KETENE ACETAL–AZONIAPOLYCYCLIC ADDUCTS

Starting azoniapolycyclic	$RCH{=}C(OEt)_2$ R	Adduct	Product	Yield,[a] %
	H	5[b]	 6[c]	95
	CH_3	7[d]	 8[e]	77
	H	9[b]	 10[c]	92
	Br	11[d]	 12[f]	73
	H	13[d]	 14[g]	97
	H	15[b]	 16[h]	83
	H	17[b]	 18[i]	45
	CH_3	19[d]	 20[j]	16

[a] Based on adduct. [b] Reference 2a. [c] A. Werner, *Justus Liebigs Ann. Chem.*, **321**, 248 (1902). [d] New adduct. See Experimental Section. [e] Mp 159–161°. *Anal.* Calcd for $C_{15}H_{12}O$: C, 86.6; H, 5.8. Found: C, 86.4; H, 5.9. [f] Mp 150–154°. *Anal.* Calcd for $C_{14}H_9BrO$: C, 61.5; H, 3.3. Found: C, 61.6; H, 3.4. [g] Mp 178–180°. *Anal.* Calcd for $C_{15}H_{12}O$: C, 86.6; H, 5.8. Found: C, 86.5; H, 6.0. [h] W. S. Rapson, *J. Chem. Soc.*, 14 (1941). [i] L. F. Fieser, *J. Amer. Chem. Soc.*, **51**, 2471 (1929). [j] Mp 262–264°. *Anal.* Calcd for $C_{21}H_{20}N_2O \cdot {}^1/_4H_2O$: C, 78.7; H, 6.4; N, 8.7. Found: C, 78.8; H, 6.4; N, 8.8.

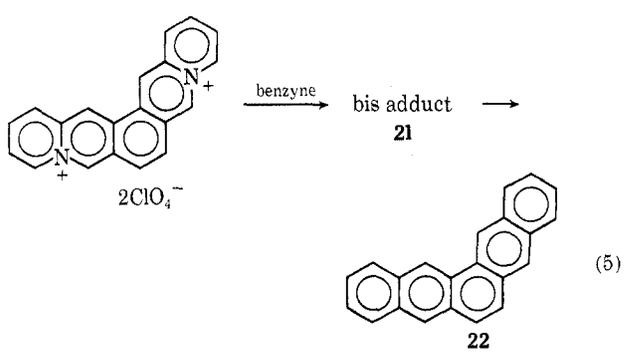
this procedure are listed in Table III. The intermediary 4a-azoniatriptycene perchlorates (**2**) have been described previously[1] and were obtained in 60–78% yields by thermal decomposition of anthranilic acid diazotized *in situ* in the presence of the appropriate 4a-azoniaanthracene perchlorate. Sodium borohydride proved to be the best reagent for the reduction step in that several attempts to catalytically hydrogenate 4a-azoniatriptycene perchlorate over PtO_2 led to a rather indiscriminate reduction of one of the benzene moieties in addition to the pyridinium ring. The thermolysis step was satisfactorily accomplished at reflux temperature in any one of several solvents, including acetic acid, acetic anhydride, and a toluene–6 *N* hydrochloric acid mixture.

TABLE III

ANTHRACENES PREPARED FROM BENZYNE–AZONIAANTHRACENE ADDUCTS

Product	Yield, %
Anthracene	93
1-Methylanthracene	94
2-Methylanthracene	87
1-Nitroanthracene	61
1-Acetoxy-4-*tert*-butylanthracene	91
1,2-Diacetoxy-4-phenylanthracene	59
9-Phenylanthracene	90

There are a number of obvious extensions of this synthesis that should be of interest, in particular the use of some of the more complex azoniapolycyclics in combinations with benzyne, substituted benzynes, other arynes, and perhaps even heteroarynes, and, in this regard, we have synthesized pentaphene from 4a,8a-diazoniapentaphene diperchlorate and benzyne (eq 5) in 31% overall yield. However, a complication in the use of substituted benzynes is anticipated, owing to a probable lack of regiospecificity[6] in a cycloaddition reaction involving a substituted benzyne with a substituted azoniaanthracene salt. It is likely that, where possible, not one but rather a mixture of two isomeric adducts will be produced, thus necessitating a separation step either at the adduct stage or after final production of the two-component anthracene mixture.



(5)

Experimental Section

Melting points (uncorrected) were determined on a Thomas–Hoover apparatus. Ultraviolet absorption spectra were recorded by a Cary Model 14 recording spectrophotometer. Nmr spectra were determined at ambient probe temperature with a Varian A-60 spectrometer. Peak positions are reported in parts per million downfield from tetramethylsilane.

New Ketene Diethyl Acetal–Azoniapolycyclic Adducts.—The new crystalline adducts tabulated in Table IV were prepared following previously described procedures.[2a]

Naphthol–Phenanthrol Synthesis. A. *Via* $NaBH_4$ Reduction.—The following example is representative of the procedure used to prepare the products listed in Tables I and II, with the exception of 1,6-diacetoxy-4-*tert*-butylnaphthalene and 1,2,6-triacetoxy-4-phenylnaphthalene. Adduct **3d** (R_3 = C_6H_5) (5.00 g, 0.011 mol) was added to a mixture of 1.50 g of sodium methoxide and 1.00 g of sodium borohydride in 50 ml of methanol in a 500-ml separatory funnel. The resulting mixture was swirled intermittently over a 5-min period and diluted with 200

TABLE IV

KETENE ACETAL-AZONIAPOLYCYCLIC ADDUCTS

Adduct	Mp, °C	Yield, %	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
3b (R_1 = C_6H_5)	160–180 dec	89	63.7	5.5	3.0	63.4	5.2	3.3
3f (R_3, R_5 = CH_3)	189–198	94	59.6	6.1	3.3	59.4	6.1	3.5
3g (R_3, R_5, R_8 = CH_3)	192–197	86	60.4	6.4	3.2	60.5	6.4	3.2
3h (R_5 = NO_2)	230 dec	93	51.3	5.1	6.3	51.7	4.8	6.3
3i (R_7 = CH_3)	133–134	94	58.6	5.9	3.4	58.6	6.0	3.5
7	199–201 dec	65	62.7	5.7	3.0	62.5	5.5	3.0
11	210–250 dec	65	52.7	4.4	2.7	52.5	4.4	2.5
13	250–290 dec	94	62.6	5.7	3.0	62.4	5.8	3.1
19	240–275 dec	73	63.4	6.0	7.4	63.3	5.8	7.5

ml of water, and the reduction product was extracted with three 50-ml portions of toluene. A mixture of the toluene extract and 50 ml of 6 *N* hydrochloric acid was refluxed for 1 hr and cooled, and the toluene layer was separated and concentrated to dryness, yielding a crystalline residue (one spot on tlc analysis). One recrystallization from methylcyclohexane afforded 2.13 g (93%) of analytically pure 3-phenyl-2-naphthol.

1,6-Diacetoxy-4-*tert*-butylnaphthalene and 1,2,6-triacetoxy-4-phenylnaphthalene were prepared by a variation of the above synthesis. As an example, adduct **3j** (R_5 = OAc, R_8 = *tert*-C_4H_9) (1.50 g, 3.2 mmol) was treated for 5 min with 0.75 g of sodium borohydride and 0.50 g of sodium methoxide in 50 ml of methanol as described above. After dilution of the reaction mixture with 200 ml of water, the solution was acidified with concentrated hydrochloric acid and then neutralized with sodium bicarbonate. The resulting precipitate was extracted with three 100-ml portions of ether and the combined extracts were concentrated to dryness, leaving a syrupy residue. This syrup was dissolved in 30 ml of 10 *N* hydrochloric acid, allowed to stand for 30 min at room temperature, and then diluted with 150 ml of water and neutralized with sodium bicarbonate. The resulting tan, amorphous solid was collected by filtration, dried, and then treated with 25 ml of acetic anhydride and 0.5 g of sodium acetate for 0.5 hr at reflux temperature. The reaction mixture was concentrated free of solvent and the residue was triturated in water, yielding a syrup. The syrup was dissolved in methylene chloride and chromatographed on a Florisil column using methylene chloride as eluent. The early fractions of eluate collected yielded the desired crystalline product, 1,6-diacetoxy-4-*tert*-butylnaphthalene, which was recrystallized as white needles (0.45 g, 47%) from ligroin (bp 60–90°): mp 101–102.5°; nmr ($CDCl_3$) δ 1.59 (s, 9, *tert*-C_4H_9), 2.30 (s, 3, OAc), 2.37 (s, 3, OAc), 7.22–8.23 (m, 5, aromatic).

B. *Via* Catalytic Reduction.—A mixture of **3i** (R_7 = CH_3) (25.0 g, 0.061 mol) in methanol (150 ml) was hydrogenated at room temperature and 66-psi initial hydrogen pressure, with PtO_2 (1.0 g) catalyst. After the consumption of 3 molar equiv of hydrogen (8 hr), when the uptake ceased, the catalyst was removed by filtration and washed with acetonitrile, and the combined filtrates were evaporated to afford 23.5 g (93%) of the crystalline perchloric acid salt of the desired reduction product. A solution of this product in 100 ml of 6 *N* hydrochloric acid was refluxed for 2 min, during which time a clear oil separated from solution. Upon cooling, the oil crystallized and was collected, recrystallized as white needles (9.50 g, 89%) from methylcyclohexane, and identified as 7-methyl-2-naphthol, mp 117–118° (lit.[8] mp 118°).

Anthracene-Pentaphene Synthesis.—With the exceptions of 1-acetoxy-4-*tert*-butylanthracene and 1,2-diacetoxy-4-phenylanthracene, the anthracenes listed in Table III were prepared following a procedure identical with that described in procedure A (*via* $NaBH_4$ reduction) of the naphthol–phenanthrol synthesis.

(8) T. G. Halsall and D. B. Thomas, *J. Chem. Soc.*, 2564 (1956).

1-Acetoxy-4-*tert*-butylanthracene.—The sodium borohydride reduction was carried out in the usual manner. However, after dilution with 200 ml of water, the reaction mixture was acidified with concentrated hydrochloric acid and neutralized with sodium carbonate; the resulting precipitate was extracted with ether. The syrup obtained by concentrating the ether extract was dissolved in 100 ml of acetic anhydride, sodium acetate (2.5 g) was introduced, and the mixture was heated for 30 min at reflux temperature. It was concentrated to a syrup, which crystallized after trituration in 100 ml of water. One recrystallization from methanol yielded the title compound as white plates (91% yield): mp 140–141°; nmr ($CDCl_3$) δ 1.65 (s, 9, *tert*-C_4H_9), 2.45 (s, 3, OAc), 7.00–8.01 (m, 6, aromatic), 8.47 (s, 1, H_9 or H_{10}), 9.00 (s, 1, H_9 or H_{10}); uv max (CH_3CN) 217 nm (log ϵ 4.07), 220 (4.06), 253 (5.16), 315 (3.08), 328 (3.46), 344 (3.76), 361 (3.94), 381 (3.89).

Anal. Calcd for $C_{20}H_{20}O_2$: C, 82.2; H, 6.8. Found: C, 81.8; H, 6.9.

1,2-Diacetoxy-4-phenylanthracene, prepared in analogous fashion, had mp 216–217°.

Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.8; H, 4.9. Found: C, 77.5; H, 5.2.

Pentaphene (22).—Crude adduct **21**[1] (5.00 g, 0.0079 mol) was introduced into a solution of sodium borohydride (3.0 g) and sodium methoxide (3.00 g) in 100 ml of methanol. After standing at autogenous temperature for 30 min, the mixture was diluted with 300 ml of water and the precipitated reduction product was extracted with two 200-ml portions of ether. The syrup obtained after concentration of the combined ether extracts was dissolved in 50 ml of acetic acid and the mixture was refluxed for 15 min, during which time golden yellow crystals separated from solution. The mixture was cooled and the product (0.68 g, 31%) collected, washed with ether, and identified as pentaphene by comparison of its melting point and spectral properties with those of an authentic sample.

Registry No.—**3b** (R_1 = C_6H_5), 30889-35-1; **3f** (R_3, R_5 = CH_3), 30889-36-2; **3g** (R_3, R_5, R_8 = CH_3), 30889-37-3; **3h** (R_5 = NO_2), 30889-38-4; **3i** (R_7 = CH_3), 30889-39-5; **7**, 30889-40-8; **8**, 30953-11-8; **11**, 30953-12-9; **12**, 18894-71-8; **13**, 30889-42-0; **14**, 30889-43-1; **18**, 30309-92-3; **19**, 31002-85-4; **22**, 222-93-5; 1-acetoxy-4-*tert*-butylanthracene, 30889-46-4; 1,2-diacetoxy-4-phenylnaphthalene, 30889-47-5; 3-phenyl-2-naphthol, 30889-48-6; 3,5-dimethyl-2-naphthol, 30889-49-7; 3,5,8-trimethyl-2-naphthol, 30889-50-0; 1,6-diacetoxy-4-*tert*-butylnaphthalene, 30310-04-40; 1,2,6-triacetoxy-4-phenylnaphthalene, 30889-52-2.

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