

78-1; 9, 22037-96-3; 12, 21991-33-3; 13, 21996-79-2; 15, 66-22-8; 16, 22027-12-9.

Acknowledgments.—F. T. R. is a member of the Chemistry and Life Sciences Laboratory of the Research Triangle Institute. Nmr spectra (HA-100)

were kindly supplied by Dr. C. G. Moreland (North Carolina State University); A-60 spectra were obtained through Mr. C. Fenske and Mr. J. Younger (Research Triangle Institute). We gratefully acknowledge and thank Dr. Thomas C. Butler, who supported this work.

Syntheses and Reactions of Phosphates from Dibromoanthrone, Anthraquinone Anil, and 1,8-Dichloroanthraquinone

JOHN S. MEEK AND LITA KOH¹

Department of Chemistry, University of Colorado, Boulder, Colorado 80302

Received May 22, 1968

10,10-Dibromoanthrone and trimethyl phosphite gave dimethyl (10-bromo-9-anthryl) phosphate, which in turn gave Diels-Alder adducts from maleic anhydride and acrylic acid. The acrylic acid adduct had the carboxylic acid group vicinal to the bridgehead bromine atom, which was verified by cleavage in hydriodic acid to the corresponding bridgehead alcohol. Dimethyl (10-anilino-9-anthryl) phosphate was formed from anthraquinone anil and methyl phosphite; no attack of trimethyl phosphite at the imino center was observed. This phosphate easily formed an adduct with maleic anhydride which was opened with hydriodic acid to yield (10-keto-9,10-dihydro-9-anthryl)succinic acid. 1,8-Dichloroanthraquinone and trimethyl phosphite in glacial acetic acid gave 1,8-dichloro-10-dimethylphosphato-9-anthrone. This reaction appears to be general, and dimethyl (4-hydroxytetrachlorophenyl) phosphate was similarly formed from chloranil and trimethyl phosphite in acetic acid.

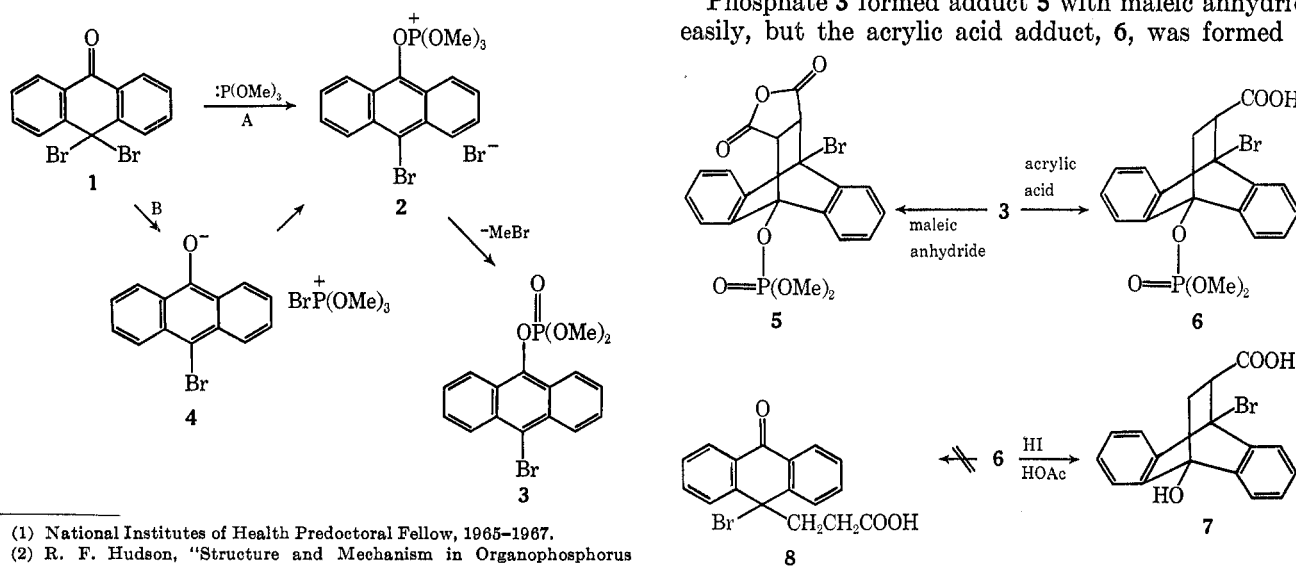
4-Bromo-2,5-cyclohexadienones have been reported to react with trialkyl phosphites to give dialkyl aryl phosphates.^{2a,3a,b} Analogous reactions are known between α -haloaldehydes, such as chloroacetaldehyde, and trialkyl phosphites, which give vinyl phosphates.^{2b,4,5} This suggests that the unstudied 10-halo-9-anthrone should react with trimethyl phosphite to give dimethyl 9-anthryl phosphates, which would provide a route to new 9,10-disubstituted anthracenes suitable for the continuation of our orientation studies in the Diels-Alder reaction.

10,10-Dibromoanthrone (1) was found to react rapidly and exothermically with trimethyl phosphite to give dimethyl (10-bromo-9-anthryl) phosphate (3) in high yield. Two mechanisms have been proposed for

this type of reaction. One (path A) involves nucleophilic attack of trimethyl phosphite at the carbonyl center to form quaternary phosphonium salt 2, which gives the product by intermolecular demethylation. The other (path B) involves attack of trimethyl phosphite on bromine to form ion pair 4 which then leads to the product *via* the same intermediate as path A.

There has been considerable discussion of these two mechanisms.^{2c,3a,6-8} Certain α -cyclohexanones are considered to react with triethyl phosphite without initial attack of phosphorus on halogen,⁸ while Miller has presented evidence that 4-bromo-2,5-cyclohexadienones go by path B.^{3b} Compound 1 can be considered to be analogous to a 4-bromo-2,5-cyclohexadienone.

Phosphate 3 formed adduct 5 with maleic anhydride easily, but the acrylic acid adduct, 6, was formed in

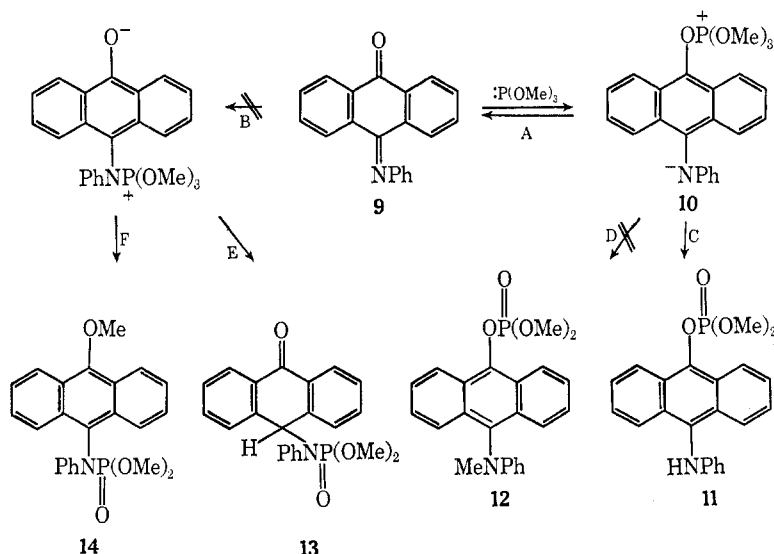


(1) National Institutes of Health Predoctoral Fellow, 1965-1967.
 (2) R. F. Hudson, "Structure and Mechanism in Organophosphorus Chemistry," Academic Press, New York, N. Y., 1965: (a) p 144; (b) pp 153-160; (c) pp 146-160.
 (3) (a) B. Miller, *J. Org. Chem.*, **28**, 345 (1963); (b) *ibid.*, **30**, 1964 (1965).
 (4) J. I. G. Cadogan, *Quart. Rev. (London)*, 208 (1962).
 (5) (a) W. Perkow, *Chem. Ber.*, **87**, 755 (1954); (b) W. Perkow, E. W. Krokow, and K. Knoevenagel, *ibid.*, **88**, 662 (1955).

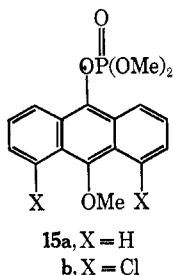
(6) (a) B. Miller, *J. Amer. Chem. Soc.*, **88**, 1841 (1966); (b) F. Ramirez, N. B. Desai, B. Hansen, and N. McKelvie, *ibid.*, **83**, 3540 (1961).
 (7) R. F. Hudson, Special Publication No. 19, The Chemical Society, London, 1965, p 93.
 (8) I. J. Borowitz, M. Ansel, and S. Firstenberg, *J. Org. Chem.*, **32**, 1723 (1967).

very low yield (17%). Acrylic acid formed only one isomer with phosphate **3**. This isomer would be predicted by steric if not electronic considerations. Hydrolysis of adduct **6** in hydriodic acid and glacial acetic acid led to the bridgehead alcohol **7**, showing the carboxylic acid group to be vicinal to the bromine atom. The other possible isomer (with carboxylic acid group vicinal to the dimethylphosphato group) would have led to the known open acid, **8**, by a previously discussed pathway.^{9,10} 9-Methoxyanthracene is known to give an adduct with acrylic acid which opens to give **8**.¹¹

Next, anthraquinone anil (**9**) was prepared from dibromide **1** and allowed to react with trimethyl phosphite in order to see if the carbonyl or imino center would be attacked preferentially by phosphorus. As expected, the more electrophilic carbonyl center was attacked (path A); but the predicted product, **12**, formed by N-methylation at intermediate stage **10**, was not formed (path D). Instead, dimethyl (10-anilino-9-anthryl) phosphate (**11**) was observed in 91% yield.



It was later discovered that very little reaction occurs and starting material is recovered if the trimethyl phosphite and anil are dried before use. This indicates that protonation of intermediate **10** occurs much faster than N methylation. Moisture, present in the reaction solution, was probably the source of the protons; when acetic acid is added at the beginning of the reaction, it proceeds smoothly at room temperature. Protonation of **9** on the nitrogen atom would facilitate the attack of trimethyl phosphite, which may explain the ready reaction in acetic acid.

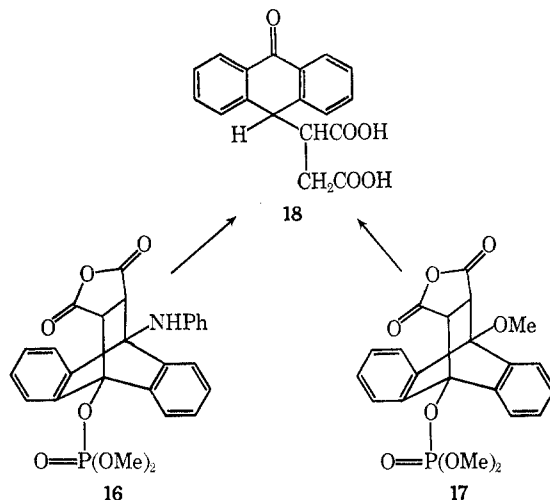


This result is in contrast to the formation of dimethyl (10-methoxy-9-anthryl) phosphate (**15a**) from anthraquinone and trimethyl phosphite.¹⁰ In this case, no protonation is observed unless acid is added externally.

The assignment of structure **11** for the product was based on the following data. Elemental analysis corresponded to an empirical formula of C₂₂H₂₀NO₄P. This formula ruled out **12** and **14** (paths D and F), respectively, as did the lack of NMe or COMe absorption in the nmr spectrum. The product showed only a doublet for the two equivalent POME groups which are split by the phosphorus.¹⁰ An infrared spectrum showed NH and no C=O absorption, which ruled out isomer **13** (path E) and confirmed structure **11**.

Compound **11** formed adduct **16** with maleic anhydride in good yield, whose nmr spectrum showed nonequivalent POME groups in agreement with Diels-Alder adducts containing a bridgehead dimethylphosphato group.¹⁰ When adduct **16** was refluxed in hydriodic acid, only the known diacid, **18**, was formed

in analogy to the reaction of adduct **17** with hydriodic acid.¹⁰ Similar ring openings with a nitrogen atom on the bridgehead have been studied in our laboratory.¹² Compound **11** did not form an acrylic acid adduct.



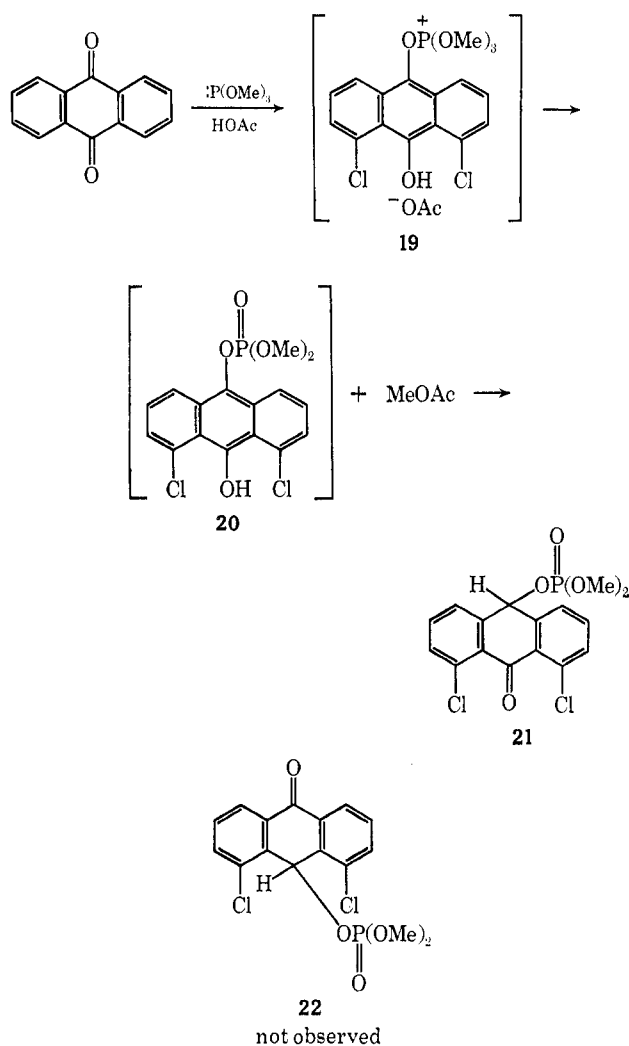
(9) J. S. Meek, P. A. Monroe, and C. J. Bouboulis, *J. Org. Chem.*, **28**, 2572 (1963).

(10) J. S. Meek and L. Koh, *ibid.*, **33**, 2942 (1968).

(11) A. W. Schultz, Ph.D. Thesis, University of Colorado, 1963.

(12) C. Loretto, Ph.D. Thesis, University of Colorado, 1965.

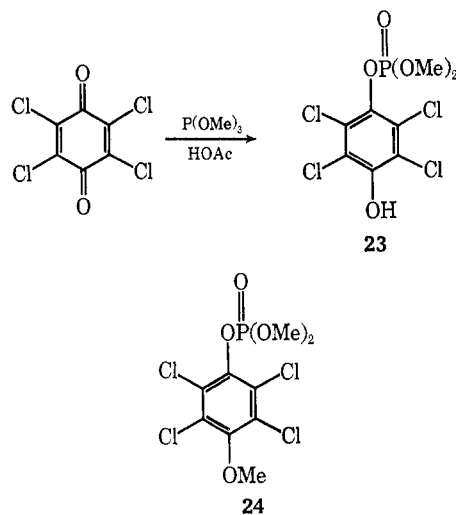
Since protonation appeared to prevent the isomerization of salt **10** to compound **12**, a similar reaction was tried with 1,8-dichloroanthraquinone by allowing it to react with trimethyl phosphite in the presence of glacial acetic acid at room temperature. It was previously found that in the absence of acetic acid, phosphate **15b** was formed.¹⁰ As expected, product **21** was isolated in high yield. This compound is easily hydrolyzed during the reaction, even at room temperature, if a large excess of acetic acid is used. Also, hydroxylic solvents hydrolyze it during recrystallization to form certain bianthrone and 1,8-dichloro-10-substituted anthrones. The dimerization of anthrones to form bianthrone and bianthrone has been discussed elsewhere.^{10,13,14}



The structural assignment for compound **21** was based on typical POME peaks in the nmr spectrum^{10,15} and carbonyl absorption in the infrared spectrum. Also, the nmr spectrum showed a doublet ($J = 11$ cps) for the C-9 proton, split by the phosphorus; the 10-OH proton would have appeared as a singlet. Finally, structure **22** was ruled out by lack of *peri*-deshielded protons observed in anthrone derivatives with protons on C-1 and C-8, *peri* to the carbonyl group.¹⁰

- (13) K. H. Meyer and A. Sander, *Ann.*, **381**, 133 (1913).
 (14) (a) E. B. Barnett and M. A. Matthews, *J. Chem. Soc.*, 2549 (1923);
 (b) E. B. Barnett, J. W. Cook, and M. A. Matthews, *Rec. Trav. Chim. Pays-Bas*, **45**, 68 (1926); (c) E. B. Barnett, N. Goodway, and J. Wiltshire, *Ber.*, **63B**, 1690 (1930).
 (15) F. Ramirez and N. B. Desai, *J. Amer. Chem. Soc.*, **85**, 3252 (1963).

This type of reaction of carbonyl compounds with trimethyl phosphite in acetic acid appears to be a general one. As mentioned above, anthraquinone anil formed phosphate **11** at room temperature under such conditions. Also, dimethyl (4-hydroxytetrachlorophenyl) phosphate (**23**)^{16a} was formed quantitatively under the same conditions. Ramirez and Dershowitz reported¹⁶ the formation of dimethyl (4-methoxytetra-



chlorophenyl) phosphate (**24**) from chloranil and trimethyl phosphite. However, they also observed a trace of compound **23** in their reaction and assumed that it formed by the pathway just discussed owing to traces of moisture in the reaction medium.^{16a}

Experimental Section

All nmr spectra were run on Varian A-60 and A-60A spectrometers using tetramethylsilane as an internal standard. Infrared spectra were obtained on a Perkin-Elmer Model 21, using KBr pellets. Melting points were obtained on a Fisher-Johns melting-point block and are uncorrected. Elemental analyses of new compounds were performed by Galbraith Laboratories, Knoxville, Tenn.

10,10-Dibromoanthrone (1).—The procedure was adapted from Goldmann's method.¹⁷ Anthrone (4 g, 7.26 mmol) was dissolved in carbon disulfide (*ca.* 250 ml). Bromine (*ca.* 4 ml) was added and the resulting solution was stirred magnetically for 2 hr. The solution was then evaporated to dryness by a stream of air, which yielded 6.86 g (94%) of straw yellow needles, mp 153–158°. Recrystallization from chloroform raised the melting point to 158° (lit.¹⁷ mp 157°). When the above reaction was carried out in chloroform, no product was obtained.

An nmr spectrum (CDCl_3) showed only a nonsymmetrical complex multiplet at 7.4–8.4 ppm. An infrared spectrum showed peaks at ν_{max} 5.98, 6.24–6.31 (d), 6.87, 7.58–7.87 (t), 10.8, and 14.5 μ .

Dimethyl (10-Bromo-9-anthryl) Phosphate (3).—Trimethyl phosphite (3 ml) was added to dibromoanthrone (1 g, 2.5 mmol). The reaction was quite exothermic and a bright yellow solution formed. After the solution had stood overnight, the excess trimethyl phosphite was removed by a stream of air. The resulting yellow crystals were washed with petroleum ether (bp 60–70°) and then chloroform to give 0.99 g (96%) of crude product, mp 80–105°. Two recrystallizations from ethanol gave bright yellow needles, mp 118–119°.

Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{BrO}_4\text{P}$: C, 50.41; H, 3.70. Found: C, 50.34; H, 3.58.

An nmr spectrum (CDCl_3) showed a doublet at 3.83 ppm (6 H, $J = 11$ cps) and two multiplets at 7.3–7.65 and 8.2–8.45 ppm (4 H). An infrared spectrum showed peaks at ν_{max} 5.93 (weak),

- (16) (a) F. Ramirez and S. Dershowitz, *ibid.*, **81**, 587 (1959); (b) F. Ramirez, E. H. Chen, and S. Dershowitz, *ibid.*, **81**, 4338 (1959).
 (17) F. Goldmann, *Ber.*, **20**, 2436 (1887).

6.3–6.53 (weak d), 6.93–7.13 (d), 7.7–7.93 (m, P=O), 9.15–9.87 (m, POC), and 11.4–11.9 μ (m).

10-Bromo-9-dimethylphosphato-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic Anhydride (5).—Dimethyl (10-bromo-9-anthryl) phosphate (**3**, 0.5 g, 1.31 mmol) was ground together with maleic anhydride (0.129 g, 1.31 mmol) dissolved in xylene (2 ml) and refluxed for 16 hr. The resulting yellow solution was concentrated under reduced pressure and the solid thus obtained was filtered and washed with pentane and chloroform to give 0.39 g (62%) of nearly white crystals which turned yellow on heating and melted at 225–235°. Recrystallization from ethanol gave an analytical sample, mp 237–244° dec.

Anal. Calcd for $C_{20}H_{16}BrO_7P$: C, 50.12; H, 3.37. Found: C, 49.81; H, 3.17.

An nmr spectrum ($CDCl_3$) showed four doublets at 4.12, 4.06 (3 H, $J = 11$ cps), 5.02, and 3.98 ppm (1 H, $J = 10$ cps) and a multiplet at 7.25–7.65 ppm (8 H) for the POMe, C-11, C-12, and aromatic protons, respectively. An infrared spectrum showed peaks at ν_{max} 5.35–5.6 (d, C=O), 8.77 (P=O), 9.1–9.9 (m, POC), and 10.4–11.8 μ (m).

10-Bromo-9-dimethylphosphato-9,10-dihydro-9,10-ethanoanthracene-11-carboxylic Acid (6).—Dimethyl (10-bromo-9-anthryl) phosphate (0.5 g, 1.31 mmol) ground together with hydroquinone (0.1 g) and *t*-butylcatechol (0.1 g) and dissolved in freshly distilled acrylic acid (1 ml) was refluxed for 1 hr. The resulting black solution solidified upon cooling. Ethyl acetate was added and the solution was filtered and washed with chloroform and pentane; the product (0.1 g, 17%) was collected. Recrystallization from ethanol gave white needles, mp 230–246° dec.

Anal. Calcd for $C_{19}H_{15}BrO_6P$: C, 50.35; H, 4.00. Found: C, 50.27; H, 3.88.

An nmr spectrum (DMSO- d_6 -acetone- d_6) showed two doublets at 3.97 and 4.00 ppm (3 H, $J = 11$ cps) and a multiplet at 7.2–8.00 ppm (8 H). The compound was nearly insoluble, even in DMSO- d_6 . An infrared spectrum showed peaks at ν_{max} 3.35 (broad, OH), 5.75, 6.9, 7.6–8.05 (m), 8.27–8.9 (m, P=O), and 9.2–9.55 μ (m, POC).

10-Bromo-9-hydroxy-9,10-dihydro-9,10-ethanoanthracene-11-carboxylic Acid (7).—The method of Meek, Monroe, and Bouboulis⁹ was used. A solution of phosphate **6** (0.48 g, 1.06 mmol) in hydriodic acid (5 ml) and glacial acetic acid (10 ml) was refluxed for 7 hr. The hot yellow solution was filtered, extracted with a large volume of ether, dried, and evaporated to give 0.1 g (27.8%) of white crystals, mp 240–254° dec. An analytical sample from acetone-petroleum ether melted at 145–154° dec.

Anal. Calcd for $C_{17}H_{13}BrO_3$: C, 60.73; H, 3.90. Found: C, 70.00; H, 3.83.

An infrared spectrum showed peaks at ν_{max} 2.93 (broad, OH), 5.85 (C=O), 6.05 (sh), 8.25–8.8 (m), and 9.1–9.5 μ (m).

Anthraquinone Anil (9).—This procedure was adapted from the method of Meyer and Sander.¹³ To a solution of 10,10-dibromoanthrone (6 g, 17.04 mmol) in chloroform (250 ml) was added aniline (5.4 ml, 3.5-fold). The resulting yellow solution was stirred magnetically at room temperature and turned bright red in 0.5 hr. Stirring was continued overnight; the solution was filtered to remove aniline hydrobromide and the filtrate was evaporated by a stream of air to give 5.32 g of red product. The product was chromatographed over a dry column of alumina [which had been deactivated by adding water (60 ml) to alumina (1 lb) and drying under reduced pressure for 8 hr], and eluted with benzene. The red anil appeared in the first fraction; 5.00 g (75%), mp 115–118°, was collected. Recrystallization from ethanol raised the melting point to 118°.

An nmr spectrum ($CDCl_3$) showed multiplets at 8.1–8.3, 6.65–6.85 (2 H), and 7.0–7.7 ppm (4 H). An infrared spectrum showed peaks at ν_{max} 6.0–6.3 (d, C=O, C=N), 6.27, 7.57–7.93 (t), and 10.7 μ .

Dimethyl (10-Anilino-9-anthryl) Phosphate (11).—A solution of anthraquinone anil (1.22 g, 4.32 mmol) in acetic acid (1 ml) and

trimethyl phosphite (2 ml) was heated on a steam bath for a few minutes and then allowed to stand overnight at room temperature. The deep red solution turned bright yellow and deposited yellow crystals. The solution was evaporated by a stream of air to a semisolid mass which, after being filtered and washed with ethyl acetate and pentane, gave 1.6 g (94% yield), mp 200° dec. Crystallization from acetone-petroleum ether gave analytically pure needles, mp 201–209° dec.

Anal. Calcd for $C_{22}H_{20}NO_4P$: C, 67.17; H, 5.12; N, 3.56. Found: C, 67.30; H, 5.27; N, 3.63.

An nmr spectrum (DMSO- d_6 - $CDCl_3$) showed peaks at 3.90 (6 H, doublet, $J = 11$ cps) and 6.4–8.4 ppm (13 H, multiplet). No NH absorption was observed. An infrared spectrum showed peaks at ν_{max} 3.05 (weak, NH), 6.25 (weak), 6.67 (weak), 7.3, 7.94, and 9.65 μ .

10-Anilino-9-dimethylphosphato-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic Anhydride (16).—Dimethyl(10-anilino-9-anthryl) phosphate (**11**, 1 g, 2.54 mmol) and maleic anhydride (0.25 g, 2.54 mmol) in xylene (2 ml) was refluxed for 18 hr. The product was purified as described above for adduct **5**. This gave 0.64 g (51.2%) of pale yellow crystals, mp 200–220° dec. Treatment with Norit followed by crystallization from acetone-petroleum ether gave analytically pure, white needles, mp 220–223° dec.

Anal. Calcd for $C_{26}H_{22}NO_7P$: C, 63.54; H, 4.51; N, 2.85. Found: C, 63.33; H, 4.45; N, 2.82.

An nmr spectrum (DMSO- d_6) showed four doublets at 4.05, 4.08 (3 H, $J = 11.5$ cps), 4.06, and 4.77 ppm (1 H, $J = 9$ cps) and a multiplet at 7.2–7.7 ppm (13 H). No NH absorption was observed. An infrared spectrum showed peaks at ν_{max} 3.03 (weak, NH), 5.87 (weak), 5.93 (sh), 6.25, 6.68–6.87 (d), 5.57–8.5 (m, P=O), 9.3–9.9 (m, POC), and 10.55–11.05 μ (t).

(10-Keto-9,10-dihydro-9-anthryl)succinic Acid (18).—Adduct **16** (0.5 g, 1.02 mmol) was treated with hydriodic acid (5 ml) as previously described. A quantitative yield of diacid **18** was obtained, mp 190–195° dec (lit.⁹ mp 194.3–195.3°). It was identified by comparison with an authentic sample.

1,8-Dichloro-10-dimethylphosphato-9-anthrone (21).—To 1,8-dichloroanthraquinone (4 g, 1.46 mmol) mixed with glacial acetic acid (2 ml) was added trimethyl phosphite (10 ml). The mixture gradually became warm, liquified, and turned red. It was stirred magnetically overnight and became a yellow semisolid. The excess trimethyl phosphite was evaporated by a stream of air and the product was filtered and washed with acetone. Pale yellow crystals (3 g, 53%) were collected after being washed well with acetone-pentane; they had mp 175–180°. Two recrystallizations from acetone-petroleum ether gave analytically pure yellow flakes, mp 181–183°. The phosphate cannot be crystallized from hydroxylic solvents due to solvolysis, and if a great excess of glacial acetic acid is used, the product is destroyed.

Anal. Calcd for $C_{16}H_{10}Cl_2O_5P$: C, 49.63; H, 3.38; N, 18.32; P, 8.00. Found: C, 49.88; H, 3.39; N, 18.28; P, 8.00.

An nmr spectrum ($CDCl_3$) showed peaks at 3.61 (6 H, doublet, $J = 11$ cps), 6.34 (1 H, doublet, $J = 8$ cps), and 7.4–7.8 ppm (6 H, multiplet). An infrared spectrum showed peaks at ν_{max} 5.9 (C=O), 6.27, 7.37, 7.75–8.45 (m, P=O), and 9.4–10.5 μ (m, POC).

Dimethyl (4-Hydroxytetrachlorophenyl) Phosphate (23).—Chloranil (1 g, 4.08 mmol) in acetic acid (1 ml) was treated with trimethyl phosphite (10 ml) as described earlier. A quantitative yield of phosphate **23** was obtained, mp 235–238° (lit.^{16a} mp 236–238°).

An nmr spectrum ($CDCl_3$) showed only a doublet at 3.96 ppm (6 H, $J = 11.5$ cps).

Registry No.—**1**, 21555-13-5; **3**, 22185-77-9; **5**, 22185-78-0; **6**, 22212-23-3; **7**, 22185-79-1; **9**, 10019-06-4; **11**, 22185-81-5; **16**, 22232-81-1; **21**, 22185-82-6; 1,8-dichloroanthraquinone, 82-43-9.