methanol–water at 25° (set 4) is 5.59, in fairly good agreement with the value of α for hydrogen–deuterium exchange in methanol–water at 21° of 7.74.

Another measure of the acidity of the ethynyl proton is provided by the data for complex formation of substituted acetylenes with diethylacetamide. The values of P_R obtained for these data (sets 5 and 7) are 35 and 36, respectively, in excellent agreement with the values of P_R obtained for hydrogen–deuterium exchange of substituted acetylenes. The magnitude of the localized effect in these sets is much smaller than that observed for hydrogen–deuterium or hydrogen–tritium exchange; the values are 1.53, 1.63, and 1.73. Obviously the complex formation is much less sensitive to substituent effects. The same effect is observed in a comparison of the magnitude of α for complex formation of 2-substituted pyridines with phenols with α for ionization of 2-substituted pyridinium ions (1.43 and 11.4, respectively).

Infrared C–H Stretching Frequencies.—The resonance effect is predominant in the majority of the sets of infrared C–H stretching frequencies, although the C–H stretching frequencies of substituted acetylenes in dimethylacetamide (set 12) show a P_R value of 34, in good agreement with those observed for hydrogen–deuterium exchange and for complex formation with diethylacetamide. There is no explanation known to us for the predominance of the resonance effect in sets 8, 9, and 11. Comparable studies of C–H stretching frequencies as a function of substituent variation do not seem to be extant for substituted benzenes or ethylenes. It should be noted that C–H stretching frequencies involve very small changes. In any case, the importance of the resonance effect in these data is obvious.

Nmr Proton Chemical Shifts.—We have previously observed that proton chemical shifts of cis and trans protons in substituted ethylenes are successfully correlated by eq 1. It therefore seemed of interest to study the proton chemical shifts of substituted acetylenes. Although significant correlations were obtained for three of the four sets studied (sets 14 , 15, and 16B), the results are not particularly good. Excluding set 16B, in which the substituents are all of the type $-CH_2X$, and therefore there is no dependence on the resonance effect, the results are in good agreement with the majority of the sets of infrared frequencies studied and in accord with the values of P_R observed for proton chemical shifts of cis and trans protons in substituted ethylenes.[13] As regards the magnitude of the resonance effect, it is larger for proton chemical shifts in substituted acetylenes (β 4.08 and 3.48 for sets 14 and 15, respectively) than it is for either trans protons (β 2.11) or cis protons (β 2.20) in substituted ethylenes.[13] As the correlation of proton chemical shifts for substituted acetylenes failed with the most extensive set of substituents studied (set 13), the conclusion we have arrived at can only be regarded as qualitative.

Conclusion

Overall, the results obtained clearly show that resonance effects are important in determining the reactivity and physical properties of the ethynyl proton. They also demonstrate the applicability of eq 1 to data for substituted acetylenes.

A Synthesis of 2,3-Dihydro-1*H*-cyclopenta[*a*]chrysene[1]

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2,3-Dihydro-1*H*-cyclopenta[*a*]chrysene (**13**) has been synthesized from 9,10-dihydrophenanthrene by a ten-step reaction sequence. The peripheral benzo ring atoms arise from succinic acid by a Haworth-type reaction sequence and the cyclopenteno atoms from carboethoxyethanoyl chloride by a Friedel–Crafts condensation, leading after several steps (**7**–**9**) to the key intermediate, 2-(3-carboxypropyl)-7-(2-carboxyethyl)phenanthrene (**10**), which was cyclized to give a mixture of products. The major constituent, established as the pentacyclic diketone, 2,3,8,9,10,11-hexahydro-1*H*-cyclopenta[*a*]chrysene-1,11-dione (**11**) by spectroscopic evidence, was converted to the final product (**13**) by reduction and dehydrogenation. Several examples of Friedel–Crafts acylation with carboethoxyethanoyl chloride are described.

In 1943 Ruzicka and coworkers[2] dehydrogenated quinovic acid and isolated among other products two aromatic hydrocarbons which were assumed to be alkylcyclopentenochrysenes. Since quinovic acid is now known to be an ursane rather than a lupane type triterpene,[3] these aromatic hydrocarbons probably have a picene rather than a cyclopentenochrysene ring system. Nevertheless it seems possible that aromatic hydrocarbons with a cyclopentenochrysene ring system could be formed, at least in small amounts, during dehydrogenation of authentic lupane type triterpenes, just as cyclopentenophenanthrene derivatives are formed by dehydrogenation of steroids. However, as yet there are no authentic reports of isolation of such substances.

Similarly, several picene type hydrocarbons, apparently formed from triterpenes during the carbonization process, have been isolated by Šorm and coworkers[4]

(1) (a) Presented in part at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 11–15, 1967. (b) Taken in part from the Ph.D. Dissertation of A. Silveira, Jr., University of Massachusetts, Amherst, Mass., 1962.

(2) L. Ruzicka, A. Grov, and G. Anner, *Helv. Chim. Acta*, **26**, 254 (1943).

(3) For a listing of the various types of triterpenes see T. G. Halsall and R. T. Aplin, *Fortschr. Chem. Org. Naturstoffe*, **22**, 153 (1964).

(4) V. Jarolim, K. Hejno, F. Hemmert, and F. Šorm, *Collect. Czech. Chem. Commun.*, **30**, 873 (1965).

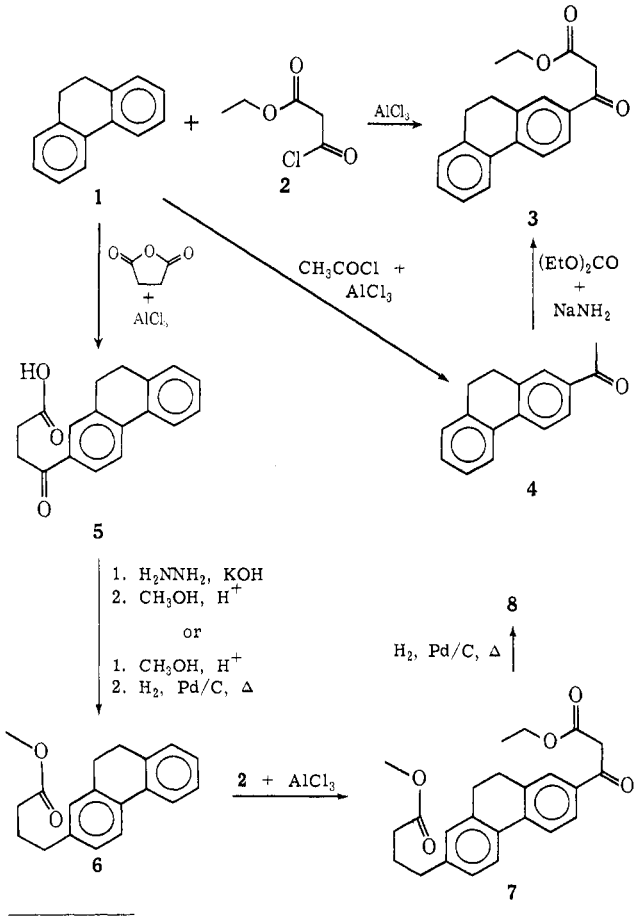
from Bohemian brown coal. Since the lupane type triterpene, betulin, is also a constituent of this coal,[5] one might reasonably expect the presence of some cyclopentenochrysene derivatives, even though to date none has been reported. In anticipation of isolation of systems of this type we have developed a synthesis of 2,3-dihydro-1*H*-cyclopenta[*a*]chyrsene (**13**) that should be applicable to the synthesis of various alkyl-substituted derivatives.

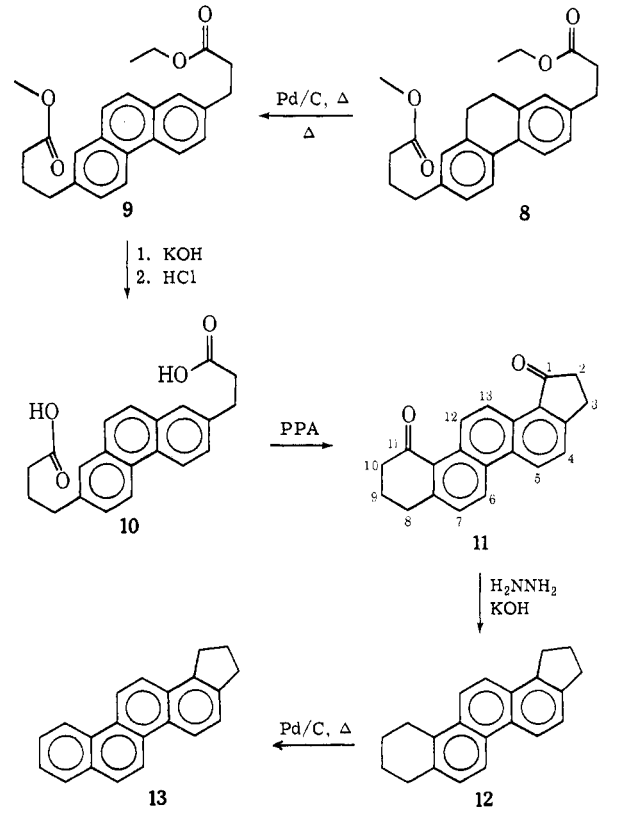
Our synthesis of **13** is based on a route to alkylpicenes described by Phillips and coworkers[6] in which the picene nucleus is built up from a phenanthrene system by Haworth-type reaction sequences which generate the two terminal benzo rings of the molecule. By appropriate modification alkyl groups may be attached to the terminal rings. Similarly, in our synthesis of **13** the three central rings are derived from phenanthrene, the terminal benzo ring from succinic acid, and the cyclopenteno ring from malonic acid. The most unique feature of the synthesis is the use of the monoester acid chloride of malonic acid as an acylating agent in a Friedel–Crafts reaction to introduce the three-carbon unit that becomes the cyclopenteno ring.

The synthesis starts with succinoylation of 9,10-dihydrophenanthrene (**1**) as previously described.[7] The resulting keto acid **5** was converted to methyl 4-(9,10-dihydro-2-phenanthryl)butanoate (**6**) by Wolff–Kishner reduction and esterification.[6a] An alternative route of catalytic hydrogenation of the methyl ester of **5** worked satisfactorily, but offered no advantage over the published one.[6a]

The next step, the introduction of the three-carbon unit that becomes the cyclopenteno ring, was accomplished by a Friedel–Crafts condensation of **6** with carboethoxyethanoyl chloride (**2**). The use of **2** as an acylating agent in Friedel–Crafts reactions was reported by Marguery[8] in 1905. He describes the formation of β-keto esters by reaction of **2** with benzene, toluene, and *p*-xylene; however, no yields are given. Since then, the reaction has found no application except for one report of its condensation with ferrocene.[9] To check the feasibility of the reaction, **2** was condensed with benzene and gave a 64% yield of ethyl benzoylacetate. Reaction of **2** with 9,10-dihydrophenanthrene (**1**) gave a 73% yield of ethyl 3-oxo-3-(9,10-dihydro-2-phenanthryl)propanoate (**3**). The same compound was prepared from the known compound 2-acetyl-9,10-dihydrophenanthrene (**4**) by base-catalyzed carboethoxylation with diethyl carbonate, thereby establishing the point of attachment of the side chain in **3** as the expected 2 position. On the basis of this result as well as the other known acylations of 9,10-dihydrophenanthrene and its derivatives,[6,7,10] all of which upon Friedel–Crafts acylation react at the 2 (or 7) position, we assume that the reaction of **6** and **2** occurs similarly, giving 2-(2-carboethoxy-1-oxoethyl)-7-(3-carbomethoxypropyl)-9,10-dihydrophenanthrene (**7**).

Catalytic reduction of the keto group in **7** gave **8**, which was dehydrogenated to **9** and then converted to the diacid 2-(3-carboxypropyl)-7-(2-carboxyethyl)-phenanthrene (**10**). Polyphosphoric acid cyclization of





(5) V. Jarolim, K. Hejno, and F. Šorm, *Collect. Czech. Chem. Commun.*, **28**, 2318 (1963).

(6) (a) D. D. Phillips, *J. Amer. Chem. Soc.*, **75**, 3223 (1953); (b) D. D. Phillips and E. J. McWhorter, *ibid.*, **77**, 3856 (1955); (c) D. D. Phillips and D. E. Tuites, *ibid.*, **78**, 5438 (1956).

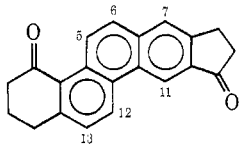
(7) D. D. Phillips and E. J. McWhorter, *ibid.*, **76**, 4948 (1954).

(8) F. Marguery, *Bull. Soc. Chim. Fr.*, **33**, 548 (1905).

(9) K. L. Rinehart, Jr., R. J. Curby, Jr., and P. E. Sokol, *J. Amer. Chem. Soc.*, **79**, 3421 (1957).

(10) W. Carruthers and D. A. Watkins, *J. Chem. Soc.*, 724 (1964).

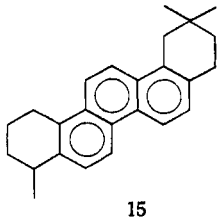
10 gave a diketone mixture from which the major component was isolated by column chromatography. Although in principle four isomers would be formed, on the basis of known examples of cyclizations of this type[6,7,10] in which the side chains invariably cyclize predominantly to the 1 and 8 positions of the phenanthrene ring, the major product should be the desired isomer, 2,3,8,9,10,11-hexahydro-1*H*-cyclopenta-[*a*]chrysene-1,11-dione (**11**). The subsequent conversion of the major product **11** to a compound with a chrysene-like uv spectrum confirms the cyclization of the four-carbon side chain of **10** to C_1 of the phenanthrene nucleus. The nmr and ir data proved that the three-carbon side chain cyclized to give **11** rather than **14**. The nmr spectrum shows doublets at δ 8.74



14

(1 H, J = 8.1 Hz) and 8.66 (1 H, J = 8.1 Hz) for the two peri hydrogens at positions 5 and 6 of **11** corresponding to the expected values near δ 8.7.[11a] These doublets require hydrogens ortho to both the C-5 H and C-6 H, thus eliminating structure **14** in which one of the peri hydrogens would appear as a singlet. Also the spectrum shows two doublets between δ 9.0 and 9.5 corresponding to the C-12 H and C-13 H of **11**. These observed downfield shifts of the C-12 and C-13 H peri to the keto function agree with values reported for similar compounds.[11b] If the compound had structure **14**, one should observe three peaks (C-5 H doublet and C-11 H singlet) in the region of δ 9.0–9.5. The integral of the other aromatic hydrogens near δ 7.5 corresponds to two protons (C-4 and C-7 H). Compound **14** would have shown three protons in this region (C-6 H, C-7 H, C-13 H). The structural assignment of **11** was substantiated by its ir spectrum, which in the region of aromatic C–H out-of-plane deformation showed absorption at 844, 813, and 803 cm^{-1} but no peaks in the 900–860-cm^{-1} region indicating no isolated aromatic C–H bonds,[12] as would be present if cyclization of **10** had occurred at other than the 1 and 8 positions.

Compound **11** was converted to the corresponding hydrocarbon **12** by a Wolff–Kishner reduction. Although **12** was not isolated in pure condition, its ir spectrum with peaks at 828 and 800 and a shoulder at 837 cm^{-1} again is consistent with the ring system of 2,3,8,9,10,11-hexahydro-1*H*-cyclopenta[*a*]chrysene. A similar structure (**15**) described by Carruthers and Watkins[10] showed but a single peak at 810 cm^{-1}. The fact that our system has five rather than six carbons in one of the peripheral rings may account for the extra peaks we observe.



15

Dehydrogenation of **12** gave the final product, 2,3-dihydro-1*H*-cyclopenta[*a*]chrysene (**13**). The uv spectrum of the compound unequivocally establishes the aromatic portion of the system as a chrysene rather than a benzanthracene unit.[13] The uv spectrum of **13** together with the nmr and ir data of the precursor diketone, **11**, fully establishes the structure of **13**. Again the ir spectrum shows peaks in the out-of-plane aromatic C–H region characteristic of sets of ortho hydrogens rather than isolated aromatic hydrogens.

The synthetic route for preparation of **13** outlined above can be applied to the preparation of alkyl-substituted cyclopentenochrysenes by introduction of alkyl groups at the ketonic functions of **5** and **11** and by substitution of the acidic hydrogen of **7**. These extensions of the synthesis as well as investigations of further applications of **2** as a Friedel–Crafts acylating agent are anticipated.

Experimental Section

All melting and boiling points were uncorrected. Uv absorption spectra were measured in MeOH using a Cary Model 14 recording spectrophotometer. Ir spectra were determined with a Perkin-Elmer Model 21 double beam spectrophotometer. Nmr spectra were determined with a Perkin-Elmer R-20 (60 MHz) instrument in $CDCl_3$ with TMS internal standard. Solids were run as KBr pellets. Elemental analyses were by Weiler and Strauss Microanalytical Laboratory, Oxford, England, and by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. The 9,10-dihydrophenanthrene was obtained from Henley and Co., New York, N. Y.

Methyl 4-(9,10-Dihydro-2-phenanthryl)butanoate (**6**).—Absolute MeOH (60 ml) and 10% Pd/C catalyst (1.0 g) were added to an electrically heated hydrogenation flask[14] containing 8.0 g (25 mmol) of methyl 4-oxo-4-(9,10-dihydro-2-phenanthryl) butanoate prepared from the acid **5** as described by Fieser and Johnson.[15] The mixture was shaken in a Parr hydrogenation apparatus at 48 psi for 12 hr at 60°. The catalyst was filtered off, the solvent was removed, and the residue was distilled, giving 5.68 g (72%) of the ester **6**, bp 230–236° (5 mm), $n^{27}D$ 1.5955.

Carboethoxyethanoyl Chloride (**2**).—Carboethoxyethanoyl chloride was prepared by the method of Breslow, Baumgarten, and Hauser.[16]

Ethyl Benzoylacetate.[8,17]—Benzene (2.58 g, 33 mmol) and carboethoxyethanoyl chloride (5.0 g, 33 mmol) dissolved in 50 ml of freshly distilled ethylene chloride were added to a 500-ml, three-necked, round-bottom flask, equipped with stirrer, addition tube for solids,[18] and reflux condenser with drying tube. To the stirred, ice-cooled solution anhydrous $AlCl_3$ (21.1 g, 158 mmol) was added over a period of 45 min. The reaction mixture was maintained at 0° for 30 min and then allowed to warm to room temperature. After 3 hr a mixture of ice and 3 N HCl was added to the reaction mixture, and the organic layer was separated, washed three times with water, and dried ($MgSO_4$). Removal of solvent and distillation gave 4.1 g (65%) of ethyl benzoylacetate, bp 142–146° (6 mm) [lit.[19] bp 132–137° (4 mm), 165–169° (20 mm)].

Ethyl 3-Oxo-3-(9,10-dihydro-2-phenanthryl)propanoate (**3**). **Method A. Acylation with Carboethoxyethanoyl Chloride.**—

(11) R. H. Martin, N. Defay, and F. Geerts-Evrard, *Tetrahedron*, **20**, 1505 (1964); *e.g.*, (a) Figures 3 and 5, compounds XXVIII and XXX; (b) Figures 2–5, compounds XX, XXI, XXVII, and XXVIII.

(12) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Wiley, New York, N. Y., 1958, p 79.

(13) M. F. Ansell, G. T. Brooks, and B. A. Knights, *J. Chem. Soc.*, 212 (1961). The uv spectrum of 1,2-dimethylchrysene is given and is very similar to that of compound **13**.

(14) R. Adams and V. Voorhees, *Org. Syn.*, **1**, 61 (1941).

(15) L. F. Fieser and W. S. Johnson, *J. Amer. Chem. Soc.*, **61**, 1647 (1939).

(16) D. Breslow, E. Baumgarten, and C. Hauser, *ibid.*, **66**, 1286 (1944).

(17) A preliminary investigation of this reaction was made by J. P. Bourgault in an undergraduate senior research project.

(18) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, Revised, D. C. Heath, Boston, Mass., 1957, p 265.

(19) R. L. Shriner, A. G. Schmidt, and L. J. Roll, *Org. Syn.*, **2**, 266 (1943).

Anhydrous $AlCl_3$ (27.8 g, 209 mmol) was added over a period of 30 min to a solution of 15.0 g (83.4 mmol) of 9,10-dihydrophenanthrene (1) and 14.7 g (98 mmol) of carboethoxyethanoyl chloride (2) in 250 ml of freshly distilled ethylene chloride cooled to 0°. The green-black reaction mixture was stirred at 0° for 3 hr and at room temperature for 6 hr and then poured with vigorous stirring into a mixture of ice and 6 *N* HCl. The organic layer was washed three times with water, dried ($MgSO_4$), and concentrated under reduced pressure in a rotary evaporator, giving 17.9 g (73%) of crude **3**. Further purification by chromatography on neutral alumina using benzene–chloroform (9:1) as eluent gave an analytical sample of **3** as a pale yellow oil: $n^{28}D$ 1.6186; uv max 252 nm (log ε 4.42), 265 (4.36), 302 (4.39); ir 735, 769, 1605, 1681, 1736, 2907 cm^{-1}.

Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.64; H, 5.96.

3. Method B. Acetylation and Carboethoxylation.—To 30 ml of tetrahydrofuran, dried and distilled over $LiAlH_4$, was added 3.90 g (100 mmol) of $NaNH_2$ (Farchan Research Laboratories, Cleveland, Ohio) and while cooling in an ice bath 11.1 g (50 mmol) of 2-acetyl-9,10-dihydrophenanthrene[20] (**4**) in 175 ml of anhydrous tetrahydrofuran was added over a 15-min period. To this stirred mixture diethyl carbonate (11.8 g, 0.10 mmol) was added dropwise over a period of 20 min. The reaction mixture was stirred at 0° for 30 min and at 55–60° for 2 hr and then poured into a slush of ice and acetic acid. The mixture was extracted with ether, the organic layer was washed with $NaHCO_3$ solution and three times with water and dried ($CaSO_4$), and the solvent was removed, leaving 10.5 g (71%) of a yellow-orange oil, $n^{28}D$ 1.6180, which has ir and uv spectra identical with those of **3** prepared by method A.

2-(2-Carboethoxy-1-oxoethyl)-7-(3-carbomethoxypropyl)-9,10-dihydrophenanthrene (7).—Anhydrous $AlCl_3$ (88.0 g, 600 mmol) was added at ice temperature over a period of 1 hr to a solution containing 48.0 g (171 mmol) of methyl 4-(9,10-dihydro-2-phenanthryl)butanoate (**6**) and 30.2 g (200 mmol) of carboethoxyethanoyl chloride (**2**) in 500 ml of purified ethylene chloride. The green-brown complex was stirred for 3 hr at 0° and for 8 hr at room temperature. The reaction mixture was poured with vigorous stirring into a mixture of 6 *N* HCl and ice. The organic layer was separated, washed three times with water, and dried ($MgSO_4$) The solvent was removed on a rotary evaporator, leaving 49.9 g (74%) of crude product which was used in the next step without further purification. In other runs yields ranged from 80 to 88%. For analytical purposes a sample of the oil was chromatographed on alumina with petroleum ether (bp 30–60°)–benzene as eluent, giving **7** as a pale yellow oil: $n^{28}D$ 1.5784; uv max 253 nm (log ε 4.49), 275 (4.34), 315 (4.36); ir 743, 820, 893, 1605, 1681, 1739, 2898 cm^{-1}.

Anal. Calcd for $C_{24}H_{26}O_5$: C, 73.07; H, 6.64. Found: C, 73.26; H, 6.43.

2-(3-Carbomethoxypropyl)-7-(2-carboethoxyethyl)-9,10-dihydrophenanthrene (8).—To an electrically heated hydrogenation flask was added 1.5 g of 10% Pd/C catalyst and 15 g (39.4 mmol) of crude ester **7** dissolved in 50 ml of anhydrous ethyl acetate. The solution was heated at about 72° and shaken for 22 hr under a pressure of 60 psi of H_2. The solution was cooled, the catalyst was filtered off, and the solvent was removed, leaving 12.3 g (85%) of a yellow oil. This oil was filtered through an alumina column using benzene–ligroin (50:50) as an eluent. The residue left on evaporation of solvent was used directly in the next reaction. For analytical purposes a small amount of the oil was chromatographed on alumina, giving ester **8** as a pale yellow oil: $n^{24}D$ 1.5570; uv max 269 nm (log ε 4.31); ir 741, 823, 881, 1736, 2898 cm^{-1}.

Anal. Calcd for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.62; H, 7.39.

2-(3-Carbomethoxypropyl)-7-(2-carboethoxyethyl)phenanthrene (9).—To 15.46 g (40.7 mmol) of ester **8** was added 0.7 g of Pd/C catalyst. The reactants were intimately mixed by heating in a water bath using a rotary evaporator and heated under N_2 on an oil bath at 270° for 6 hr, the melt was dissolved in benzene, the catalyst was filtered off, and the solution was run through an alumina column. Evaporation of solvent gave 11.6 g (75.5%) of oily product. Further chromatography on alumina using benzene–ligroin as eluent gave an analytical sample of the ester **9** as a pale yellow oil: $n^{27}D$ 1.5821; uv max 253 nm (log ε 4.93), 277 (4.40), 296 (4.11); ir 717, 746, 813, 833, 889, 1623, 1739, 2898 cm^{-1}.

(20) A. Burger and E. Mosettig, *J. Amer. Chem. Soc.*, **58**, 1857 (1936).

Anal. Calcd for $C_{24}H_{26}O_4$: C, 76.16; H, 6.93. Found: C, 76.32; H, 7.18.

2-(3-Carboxy-1-propyl)-7-(2-carboxyethyl)phenanthrene (10).—To a solution containing 4.2 g of 85% KOH dissolved in 50 ml of MeOH was added 11.6 g (61.4 mmol) of ester **9** dissolved in 80 ml of MeOH. After refluxing on a steam bath for 6 hr the solvent was removed and 125 ml of water was added to give a clear orange solution. After three extractions with ether the water layer was briefly heated on a steam bath, then chilled in ice and slowly poured into an ice–6 *N* HCl slush. The precipitated acid **10** was filtered and dried to give 9.18 g (88.5%) of gray powder, mp 209–211°. Recrystallization from acetic acid gave white, powdery crystals, mp 213–216°. After a further recrystallization from CH_3OH and five recrystallizations from acetic acid an analytical sample was obtained: mp 217–219°; uv max 256 nm (log ε 4.96), 278 (4.27), 297 (3.89); ir 714, 816, 897, 1698, 2898 (broad), 3390 cm^{-1}.

Anal. Calcd for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 74.68; H, 6.35.

2,3,8,9,10,11-Hexahydro-1*H*-cyclopenta[*a*]chrysene-1,11-dione (11).—Polyphosphoric acid (60 g) was added with stirring to 1.5 g (4.4 mmol) of acid **10**, mp 213–216°. The temperature rose slightly and the mixture became yellow-orange in color. The flask was gradually heated to 60° in an oil bath and held at this temperature for 48 hr. The color gradually changed from yellow-orange to red. The reaction mixture was poured into a water–ice slurry with vigorous stirring, giving a dark red solid which was collected and washed with water, then dissolved in $CHCl_3$. The solution was extracted four times with $NaHCO_3$ solution and four times with water and dried ($MgSO_4$). Acidification of the $NaHCO_3$ extract gave no precipitate. Evaporation of the solvent left a red solid which was dissolved in a 9:1 benzene–chloroform mixture and chromatographed on 50 g of neutral alumina. Elution with 9:1 and 8:2 benzene–chloroform solutions gave 0.11 g of solid, mp 189–193°. Later fractions obtained by elution with 6:4 and 4:6 benzene–chloroform solutions had mp 212–215° and totaled 0.70 g (52%). Further purification of the higher melting material by filtration of a $CHCl_3$ solution of it through alumina, evaporation of solvent, and recrystallization first from acetic acid, then three times from acetone, and finally from MeOH produced pale yellow flakes of **11**: mp 221–223°; uv max 261 nm (log ε 4.80), 320 (4.32); ir 803, 813, 844, 1664, 1692, 2898 cm^{-1}; nmr δ 9.43 (d, 1 H, J = 9.6 Hz, C-12 H), 9.23 (d, 1 H, J = 9.6 Hz, C-13 H), 8.74 (d, 1 H, J = 8.1 Hz, C-6 H), 8.66 (d, 1 H, J = 8.1 Hz, C-5 H), 7.59 (d, 1, H, J = 8.1 Hz, C-4 H), 7.45 (d, 1 H, J = 8.1 Hz, C-7 H), 3.1 (m, 4 H, $ArCH_2$), 2.7 (m, 4 H, $COCH_2$), 2.2 (m, 2 H, $CH_2CH_2CH_2$). (The assignment of C-6 H, C-5 H, C-4 H, and C-7 H is not entirely certain; it might be C-5 H, C-6 H, C-7 H, and C-4 H in order of increasing field strength.)

Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.97; H, 5.37. Found: C, 84.03; H, 5.47.

In subsequent runs the main fraction from chromatography melted at 211–214° and 214–217°, respectively, in two separate runs. Recrystallization from MeOH gave product of mp 218–221°. The corresponding minor fraction, mp 186–205° and 187–203°, respectively, apparently was a mixture. The ratio of main product to minor fraction was about 6:1.

2,3-Dihydro-1*H*-cyclopenta[*a*]chrysene (13).—Compound **11** (400 mg, 1.33 mmol), mp 214–217°, was dissolved in 15 ml of diethylene glycol; 0.5 ml of 85% hydrazine was added; and the mixture was refluxed for 3 hr. The red solution was cooled to 90° and 0.51 g (9.1 mmol) of KOH dissolved in 6 ml of diethylene glycol was added. After refluxing for 1.5 hr (175°) the condenser was removed and the temperature was allowed to rise to 195°, when refluxing was continued for 4 hr longer. Addition of an ice–water mixture to the cooled contents of the flask gave a dark red precipitate, which after washing with water and drying produced 0.35 g (96%) of a gray powder, mp 185–190°. Recrystallization, first from 95% EtOH, then from ligroin gave pale yellow, powdery crystals: mp 197–199° uv max 264 nm (log ε 4.97), 285 (4.32), 295 (4.27), 308 (4.38); ir 800, 828, 837 (sh), 2898 cm^{-1}. This material, **12**, was used without further purification in the subsequent dehydrogenation. Crude **12** (100 mg, 0.36 mmol), mp 197–199, was intimately mixed with 30 mg of 10% Pd/C in a test tube and heated under N_2 in a bath initially at 220°. The bath was gradually raised to 270° and held at that temperature for 1 hr. During this time white, mica-like flakes formed on the sides of the tube. These were removed and dissolved in EtOH, and the solution was filtered through alumina. Recrystallization from EtOH gave 6 mg of **13**: mp 260–261°; uv max 263 nm (log

ϵ 4.83), 272 (5.21), 297 (4.27), 308 (4.28), 324 (4.22), 347 (3.49), 364 (3.29) ir 743, 778, 801, 860 (w), 1255 (w), 2898 cm^{-1}.

Anal. Calcd for $C_{21}H_{16}$: C, 93.99; H, 6.01. Found: C, 94.11; H, 6.13.

The remainder of the product was recovered directly from the reaction mixture by vacuum sublimation, giving 42 mg (42%) of **13** as a white powder, mp 256–261°.

Registry No.—**3**, 35639-14-6; **6**, 35639-15-7; **7**, 35639-16-8; **8**, 35639-17-9; **9**, 35639-18-0; **10**, 35639-19-1; **11**, 35639-20-4; **13**, 35639-21-5; ethyl benzoylacetate, 94-02-0.

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Studies of the Synthesis of Cephalotaxine. I

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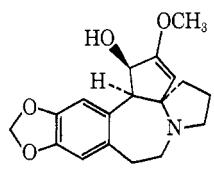
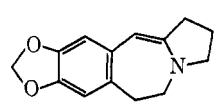
An attempted synthesis of cephalotaxine is described. The key intermediate, 8,9-methylenedioxy-1,2,3,6-tetrahydro-5*H*-pyrrolo[2,1-*b*][3]benzazepine (**1**) was obtained by a six-step sequence from *N*,*N*-dimethylpiperonylamide and pyrrole. Annelation of **1** with ethyl γ-bromoacetoacetate afforded a rearrangement product, 11,12-methylenedioxy-2-oxo-3-carboethoxy-2,3,3a,4,5,6,8,9-octahydro-1*H*-benzo[*a*]cyclopenta[*i*]quinolizine (**10**), rather than the expected product **8** bearing the cephalotaxine skeleton. Hydrolysis of **10** yielded 11,12-methylenedioxy-2-oxo-2,3,3a,4,5,6,8,8-octahydro-1*H*-benzo[*a*]cyclopenta[*i*]quinolizine (**11**), which was reduced to yield 11,12-methylenedioxy-2,3,3a,4,5,6,8,9-octahydro-1*H*-benzo[*a*]cyclopenta[*i*]quinolizine which was identical with authentic material.

Cephalotaxine and several closely related compounds have been isolated from several species of the *Cephalotaxacea* family.[1] The structure of cephalotaxine was deduced from its spectroscopic properties[2] and an X-ray crystallographic study.[3] In particular, the harringtonines which are naturally occurring esters of cephalotaxine have shown promising antileukemic activity.[4] Neither the acid portion of the harringtonines nor cephalotaxine show antileukemic activity alone. However, cephalotaxine presents the more difficult synthetic problem.



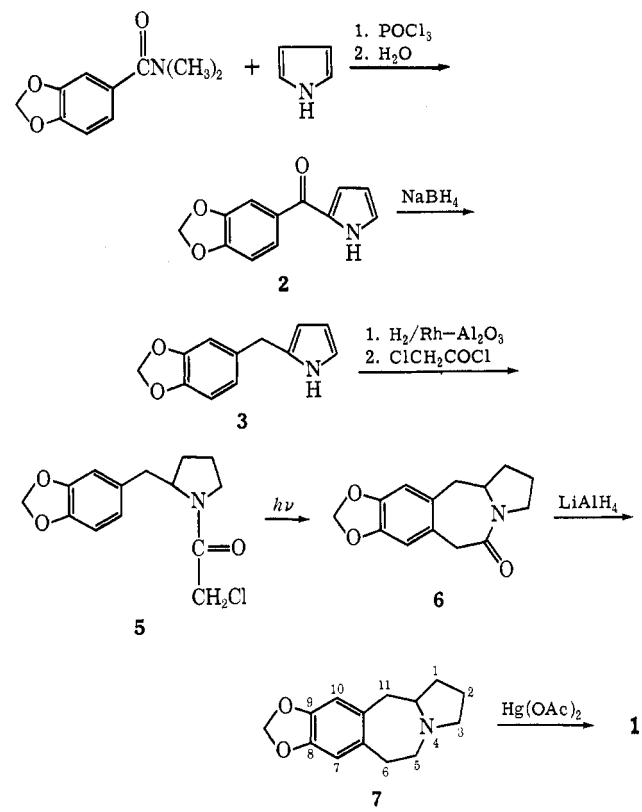
cephalotaxine

An attractive approach to the synthesis of cephalotaxine involves the annelation of the tricyclic enamine **1**, which was obtained by the sequence outlined in Scheme I.



1

SCHEME I



The sequence leading to the enamine **1** proceeds smoothly and none of the steps is exceptional. The Vilsmeier–Haack condensation[5] between *N*,*N*-dimethylpiperonylamide and pyrrole affords the 2-acylpyrrole **2** in 80% yield. Removal of the ketonic oxygen by treatment with sodium borohydride gives the benzylpyrrole **3** in 60% yield. Hydrogenation of the pyrrole ring and acetylation with chloroacetyl chloride give good yields of the chloroacetamide **5**. Photolytic cyclization of the chloroamide affords the benzazepine derivative **6** in 25% yield.[6] The structure of this material is supported by its spectroscopic properties.

(1) W. W. Paudler, G. I. Kerley, and J. McKay, *J. Org. Chem.*, **28**, 2194 (1963).

(2) R. G. Powell, D. Weisleder, C. R. Smith, Jr., and I. A. Wolff, *Tetrahedron Lett.*, 4081 (1969).

(3) D. J. Abraham, R. D. Rosenstein, and E. L. McGandy, *ibid.*, 4085 (1969).

(4) R. G. Powell, D. Weisleder, C. R. Smith, Jr., and W. K. Rohwedder, *ibid.*, 815 (1970).

(5) G. H. Cooper, *J. Org. Chem.*, **36**, 2897 (1971).

(6) O. Yonemitsu, Y. Okuno, Y. Kanaoka, and B. Witkop, *J. Amer. Chem. Soc.*, **92**, 5686 (1970).