Methylation of this coumarin yielded the same trimethyl ether as above. M.p. and mixed m.p. 178°.

Demethylation of the dimethoxycoumarin (0.5 g.) with hydriodic acid (5 ml.; 1.7 d.) by refluxing for 2 hr. in acetic anhydride solution (5 ml.) gave 4,7,8-trihydroxycoumarin. M.p. and mixed m.p. with the product described above was 258° (dec.).

3,3'-Methylene bis-(4-hydroxy-7,8-dimethoxycoumarin). White needles from cyclohexanone, m.p. 288° (dec.).

Anal. Calcd. for $C_{23}H_{20}O_{10}$: C, 60.5; H, 4.4. Found: C, 60.8; H, 4.4.

Elbs persulfate oxidation of 4,7,8-trimethoxycoumarin. 4,7,8-Trimethoxycoumarin (1 g.) was dissolved in sodium hydroxide (10%; 20 ml.) by heating on a steam bath. The solution was then cooled and potassium persulfate (1.5 g. in 30 ml. water) was added gradually during 3 hr. The solution was mechanically stirred and the temperature was not allowed to rise above 10°. The reaction mixture was left overnight and next day it was just acidified with hydrochloric acid and extracted with ether. The ether on evaporation gave negligible product. To the aqueous layer more concentrated hydrochloric acid (30 ml.) was added and the solution heated on a steam bath for 4 hr. It was then extracted with benzene in the cold. The product obtained on removal of benzene crystallized from water in pale yellow prisms, m.p. 119°. Mixed melting point with an authentic specimen of 2,5-dihydroxy-3,4-dimethoxyacetophenone[10] was not depressed.

Elbs persulfate oxidation of 4,7-dimethoxy coumarin. 4,7-Dimethoxycoumarin[1] on similar oxidation gave a product m.p. 164°. Mixed m.p. with an authentic specimen of 2,5-dihydroxy-4-methoxyacetophenone[11] was not lowered.

2-Hydroxy-4-methoxybenzoylacetic acid. 4,7-Dimethoxycoumarin (0.5 g.) was heated with sodium hydroxide solution (10%; 20 ml.) on a steam bath for 30 min. The resulting solution was then cooled and acidified with dilute ice cold hydrochloric acid. The precipitated solid (0.35 g.) melted at 126–128° (effervescence). It dissolved in sodium bicarbonate solution with effervescence. It gave a reddish brown color with alcoholic ferric chloride.

Anal. Calcd. for $C_{10}H_{10}O_5$: C, 57.1; H, 4.8. Found: C, 57.5; H, 4.9.

(11) Bargellini and Aureli, *Atti. accad. Lincei*, 20 (*ii*), 118 (1911).

(a) The above acid (0.3 g.) was heated for 15 min. on a water bath with hydrochloric acid (1:1) and the product obtained crystallized from dilute alcohol in needles, m.p. 256°. Mixed m.p. with 4-hydroxy-7-methoxycoumarin[2] was not lowered. (b) The above acid (0.3 g.) was heated with water (20 ml.) on a steam bath for 2 hrs. The reaction mixture was cooled and extracted with ether (40 ml.). The ether extract was washed with sodium bicarbonate solution (5%; 20 ml.). The sodium bicarbonate solution on acidification gave 4-hydroxy-7-methoxycoumarin. The ether on evaporation gave 2-hydroxy-4-methoxyacetophenone as seen by direct comparison.

2-Hydroxy-3,4-dimethoxybenzoylacetic acid. Obtained from 4,7,8-trimethoxycoumarin by the action of alkali as above, m.p. 123°. It dissolved in sodium bicarbonate solution with effervescence. It gave a reddish brown color with alcoholic ferric chloride.

Anal. Calcd. for $C_{11}H_{12}O_6$: C, 55.0; H, 5.0. Found: C, 54.9; H, 4.7.

On heating with hydrochloric acid (1:1) it gave 4-hydroxy-7,8-dimethoxycoumarin and on heating with water on a steam bath for 2 hr. it gave two products: 4-hydroxy-7,8-dimethoxycoumarin and 2-hydroxy-3,4-dimethoxyacetophenone.[10]

Action of hydrochloric acid on various 4-methoxycoumarin derivatives. (a) A mixture of 4,7-dimethoxycoumarin (0.3 g.) and hydrochloric acid (1:1; 10 ml.) was heated on a steam bath for 0.5 hr. The product obtained on cooling crystallized from dilute alcohol in needles, m.p. 256°. Mixed m.p. with 4-hydroxy-7-methoxycoumarin[2] was not depressed.

(b) 4,7,8-Trimethoxycoumarin (0.3 g.) on similar treatment with hydrochloric acid (1:1; 10 ml.) gave 4-hydroxy-7,8-dimethoxycoumarin as seen by direct comparison with the product described above.

(c) 4,6-Dimethoxycoumarin[8] (0.3 g.) on similar treatment with hydrochloric acid (1:1; 10 ml.) gave 4-hydroxy-6-methoxycoumarin[8] as seen by direct comparison.

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BARODA 1, INDIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF TEMPLE UNIVERSITY]

Substituted 1,10-Phenanthrolines. X. Ethyl Derivatives[1]

FRANCIS H. CASE, ZELDA B. JACOBS, RICHARD S. COOK, AND JACK DICKSTEIN

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The preparation of the following compounds, together with necessary intermediates, is described: 3-, 4-, and 5-ethyl-1,10-phenanthrolines; 3,8-; 4,6-; 4,7-; and 5,6-diethyl-1,10-phenanthrolines.

In view of the results of recent analytical tests on methyl-1,10-phenanthrolines[2] it was considered of interest to prepare some of the homologous ethyl derivatives.

The use of 1-chloropentanone-3, $ClCH_2CH_2COC_2H_5$, in the synthesis of a quinoline was first reported by Blaise and Maire,[3] who prepared 4-ethylquinoline from aniline and aniline hydrochloride in ethanol solution using this reagent. We have found that it may be used satisfactorily as component B in a modified Skraup reaction (Yale[4] method) for the preparation of 4-ethyl-

(1) This work was supported by a grant from the Committee on Research and Publications of Temple University.

(2) W. W. Brandt and G. F. Smith, *Anal. Chem.*, 21, 1313 (1949).

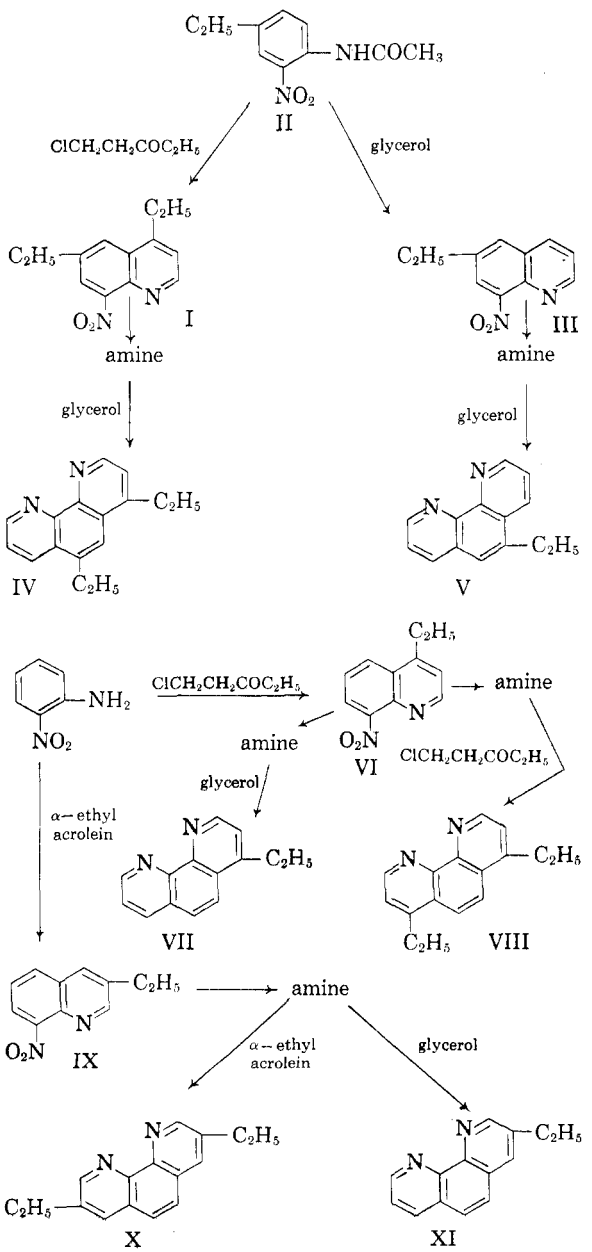
(3) E. E. Blaise and N. Maire, *Bull. soc. chim. France*, [4] 3, 662, 667 (1908).

(4) H. L. Yale and J. Bernstein, *J. Am. Chem. Soc.*, 70, 254 (1948).

quinolines and 4-ethyl-1,10-phenanthrolines.

The synthesis of 3-ethylquinoline by the action of α-ethylacrolein on aniline in a Skraup reaction has been reported by Utermohlen.[5] We have found that this reagent may be used advantageously under the conditions of a modified Skraup reaction to prepare certain substituted 3-ethylquinolines and phenanthrolines.

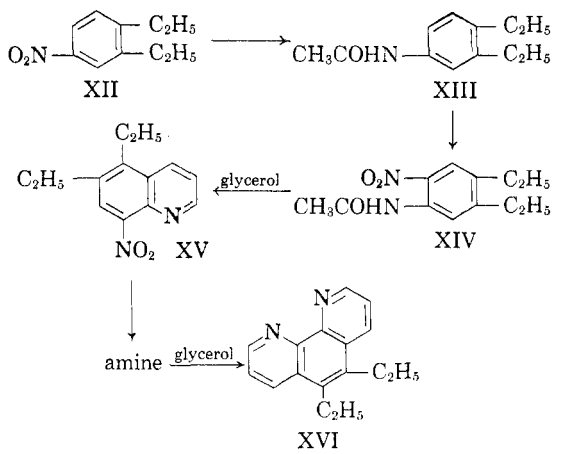
For the synthesis of 5-ethyl-1,10-phenanthroline (V), 4-ethyl-2-nitroacetanilide (II) was treated with glycerol in a Skraup reaction, yielding 6-ethyl-8-nitroquinoline (III). Reduction to the amine, followed by a second Skraup reaction yielded (V). Treatment of (II) with 1-chloropentanone-3 in a modified Skraup reaction yielded 4,6-diethyl-8-nitroquinoline (I). Reduction to the amine, followed by the usual type of Skraup reaction yielded, 4,6-diethyl-1,10-phenanthroline (IV).



By the action of *o*-nitroaniline with 1-chloropentanone-3 in a modified Skraup reaction we obtained 4-ethyl-8-nitroquinoline (VI). Reduction to the amine followed by a Skraup reaction involving glycerol yielded 4-ethyl-1,10-phenanthroline (VII). Treatment of the above amine with 1-chloropentanone-3 produced 4,7-diethyl-1,10-phenanthroline (VIII).

A modified Skraup reaction involving *o*-nitroaniline and α-ethylacrolein afforded 3-ethyl-8-nitroquinoline (IX), which was reduced to the amine. A Skraup reaction using glycerol yielded 3-ethyl-1,10-phenanthroline (XI). From a modified Skraup reaction with α-ethylacrolein, 3,8-diethyl-1,10-phenanthroline (X) resulted.

For the preparation of 5,6-diethyl-1,10-phenanthroline, pure *o*-diethylbenzene was prepared from *o*-bromoethylbenzene and ethyl magnesium bromide.[6] Nitration according to the method of Lambooy[7] yielded 1,2-diethyl-4-nitrobenzene (XII) from which 3,4-diethylacetanilide[7] (XIII) was obtained. Nitration of (XIII) yielded 4,5-diethyl-2-nitroacetanilide (XIV). The free amine obtained on hydrolysis of XIV was identical with a product of proven structure obtained by Lambooy from the hydrolysis of the nitration product of 3,4-diethylcarbethoxyanilide. Treatment of (XIV) with glycerol in a Skraup reaction yielded 5,6-diethyl-8-nitroquinoline (XV), which, after reduction to the amine, was converted by a second Skraup reaction into 5,6-diethyl-1,10-phenanthroline (XVI).



EXPERIMENTAL

α-Ethylacrolein. This was prepared by the method of Marvel *et al.*[8]

1-Chloropentanone-3. The procedure was the same as that of Utermohlen[5] except that chloroform was substituted for nitrobenzene.

(5) W. P. Utermohlen, *J. Org. Chem.*, **8**, 544 (1943).

(6) J. V. Karabinos, K. T. Serijan, and L. C. Gibbons, *J. Am. Chem. Soc.*, **68**, 2107 (1946).

(7) J. P. Lambooy, *J. Am. Chem. Soc.*, **71**, 3756 (1949).

(8) C. S. Marvel, R. L. Myers, and J. H. Saunders, *J. Am. Chem. Soc.*, **70**, 1694 (1948).

TABLE I
8-NITROQUINOLINES

Substituent	Method	1st Component -aniline	2nd Component	M.P., °C.	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
3-ethyl[a]	H_3PO_4	2-nitro-	EA	89–90	23	65.33	65.61	4.98	4.74
4-ethyl[b]	H_3PO_4	2-nitro-	CP	96–7	55	65.33	65.45	4.98	4.97
6-ethyl[c]	H_2SO_4	4-ethyl-2-nitro-	G	82–3	55	[d]			
4,6-diethyl[b]	H_3PO_4	4-ethyl-[e] 2-nitro-	CP	84–5	46	67.81	67.60	6.13	6.19
5,6-diethyl[f]	H_2SO_4	4,5-diethyl-2-nitro-	G	95–6	63	67.81	67.72	6.13	6.16

Crystallized from [a] methanol; [b] benzene–petroleum ether; [c] ethanol-water; [d] *Anal.* Calcd.: N, 13.85. Found: N, 13.45 [e] Acetyl derivative used. [f] petroleum ether.

In Tables I and II, G = glycerol; EA = α-ethylacrolein; CP = 1-chloropentanone-3.

TABLE II
1,10-PHENANTHROLINES

Substituent	Method	1st Component 8-Amino-quinoline	2nd Component	M.P., °C.	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
3-ethyl	H_2SO_4	3-ethyl	G	144–5	47	80.74	81.10	5.81	5.81
4-ethyl	H_2SO_4	4-ethyl	G	108–9	18	80.74	80.82	5.81	5.80
5-ethyl	H_2SO_4	6-ethyl	G	80–1	14	80.74	80.69	5.81	5.99
3,8-diethyl	H_3PO_4	3-ethyl	EA	112–13	16	81.32	81.43	6.83	6.80
4,6-diethyl	H_2SO_4	4,6-diethyl	G	130–1	19	81.32	81.39	6.83	6.73
4,7-diethyl	H_2SO_4	4-ethyl	CP	116–17	27	81.32	81.22	6.83	6.79
5,6-diethyl	H_2SO_4	5,6-diethyl	G	161–2	44	81.32	81.27	6.83	6.90

TABLE III
8-AMINOQUINOLINES

Substituent	M.P. or B.P., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
3-ethyl	b.p. 151–4(2 mm.)	76.71	76.19	7.02	6.74
4-ethyl	m.p. 60–61[a]	76.71	76.85	7.02	7.08
6-ethyl	b.p. 161–2 (6 mm.)	[b]			

[a] Crystallized from ethanol-water. [b] *Anal.* Calcd.: N, 16.27. Found: N, 16.69.

4-Ethyl-2-nitroacetanilide. The following method was found superior to that recorded in the literature.[9] *p*-Ethylacetanilide (33.7 g. or 0.2 mole) was added, with stirring, in 1- to 2-g. portions to 122 g. of nitric acid (sp. g. 1.45). When the temperature had risen to 40° the material was cooled in an ice bath and the rest of the anilide was added at such a rate that the temperature remained at 35–40°. After all the *p*-ethylacetanilide had been added, the mixture was allowed to stand for about 15 min. and was then poured upon crushed ice. The oily organic layer was dissolved in about 100 ml. of benzene and separated from the aqueous layer, which was then extracted with two 50-ml. portions of benzene. The combined extracts were dried over anhydrous sodium sulfate and the benzene was distilled off. Crystallization of the crude oil from low-boiling petroleum ether gave 32.3 g. (74%) of 4-ethyl-2-nitroacetanilide, m.p. 45–47° (lit., 45–47°[9]).

o-Bromoethylbenzene. In the absence of suitable directions in the literature the following procedure was used. Freshly distilled *o*-ethylaniline (b.p. 82.0°/7 mm.) (153.0 g. or 1.25 moles) was added slowly with stirring to 1215 g. (6.0 moles) of 40% hydrobromic acid over a period of 1 hr. at 20–30°. The thick slurry was cooled to 5° and 121.0 g. (1.7 moles) of sodium nitrite (97%) added with stirring in 5- to 10-g. portions over a period of 1 hr. at 5–10°. Copper powder (5.0 g.) was added and the mixture was heated to 30° to start the decomposition of the diazonium salt. After decomposition started the temperature was maintained at 15° for 1 hr. and then raised to 90–95° for 30 min. After adding 1 l. of water the mixture was steam distilled. The distillate was made basic with 5 to 10 g. of solid sodium hydroxide and extracted with 500 ml. of benzene, washed twice with 500-ml. portions of 10% sodium hydroxide, thrice with 500-ml. portions of water and dried over anhydrous sodium sulfate. The benzene was removed by distillation at reduced pressure yielding 140.0 g. of crude product. Distillation through a 15-inch packed column gave 111.0 g. of slightly yellow oil which boiled at 64° (8.0 mm.); n_D^{20} 1.5487 (reported[6] 1.5492). The yield was 48% of theory.

Anal. Calcd. for C_8H_9Br: Br, 43.3. Found: Br, 42.6.

On acidification of the alkaline washings, 29 g. of *o*-ethylphenol, b.p. 88–90° (13 mm.) was obtained.

o-Diethylbenzene. Since no detailed directions for this method could be found in the literature, the following procedure was used. In a 1-l. three-neck flask fitted with stirrer, thermometer, dropping funnel, and condenser, was placed 12.4 g. (0.508 mole) of magnesium. The system was then flushed with nitrogen. A solution of 77.8 g. (0.420 mole)

(9) H. Paucksch, *Ber.*, **17**, 767 (1884).

of *o*-bromoethylbenzene in 200 ml. of dry ether was then added slowly. Reaction started at once. The temperature was moderated by cooling so that a mild reflux was maintained. After the addition was complete (1 hr.) the mixture was refluxed for 2 hr. Freshly distilled diethylsulfate (126 g., or 0.820 mole) in 200 ml. of dry ether was then added with cooling at such a rate that a mild reflux was maintained. After further refluxing for 2 hr. the mixture was poured into 200 ml. of ice cold 10% sulfuric acid. The ether layer was washed with 200 ml. of 10% sulfuric acid, five times with 500-ml. portions of water, and dried over anhydrous sodium sulfate. Removal of ether and fractional distillation yielded 32.5 g. (57.8%) of an oil boiling at 70–73° (17 mm.); n_D^{20} 1.5033 (lit.[6] 1.5034).

General procedure for the synthesis of 8-nitroquinolines and 1,10-phenanthrolines.

A. Use of sulfuric acid. A stirred mixture of one molar proportion of the appropriate aromatic amine, 1 mole of arsenic acid hemihydrate, 4 moles of sulfuric acid in 96.8% solution (10 moles in the preparation of 3-ethylphenanthroline) and a volume of water equal to one third of the volume of sulfuric acid used was heated to 100° and treated with 3.5 moles of glycerol or 2 moles of 1-chloropentanone-3 at such a rate that the temperature did not exceed 140°. Heating was continued at this temperature for 2 hr. (25 min. in the preparation of 5,6-diethylphenanthroline). The mixture was then poured into water, made alkaline, and the precipitate removed by filtration. Both filtrate and precipitate were extracted with hot benzene. After removal of the solvent the 8-nitroquinolines prepared by this method were crystallized from the solvents indicated in Table I. The phenanthrolines were all crystallized from benzene–petroleum ether except 5,6-diethyl-1,10-phenanthroline for which petroleum ether alone was used.

B. Use of phosphoric acid. A stirred mixture of one molar proportion of aromatic amine, 2 moles of arsenic acid hemihydrate and 85% phosphoric acid (100 ml. per 0.1 mole of amine) was heated to 100° and 1-chloropentanone-3 (1.3 moles) or α-ethylacrolein (2 moles) added dropwise at such a rate that the temperature did not exceed 105°. This temperature was maintained for an additional 0.5 hr. The reaction mixture was then poured on ice and neutralized with concentrated ammonium hydroxide. The resulting precipitate and filtrate were extracted with hot benzene, and the combined extracts evaporated to dryness. The 8-nitroquinolines prepared by this method were crystallized from the solvents indicated in Table I. 3,8-Diethylphenanthroline was crystallized from benzene–petroleum ether.

8-Aminoquinolines. These were all prepared by the catalytic reduction (Adams' catalyst) of the corresponding 8-nitroquinolines except 4,6-diethyl-8-aminoquinoline for which stannous chloride in ethanol was used as the reducing agent. 4,6-Diethyl- and 5,6-diethyl-8-aminoquinolines were oils which were used directly for the preparation of the phenanthrolines, without further purification.

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PHILADELPHIA, PA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Steric Requirements in the Cyclization of Naphthalene Derivatives

CARL DJERASSI AND GEORGE R. PETTIT[1]

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While polyphosphoric acid cyclization followed by dehydrogenation of γ-(2-naphthyl)butyraldehyde (Ia) yields exclusively phenanthrene, the corresponding substituted ketones Ib, Ic and Id lead predominantly to linear cyclization products of the anthracene series. These results are ascribed to steric interference of the 4 and 5 substituents in the phenanthrene series and are not operative in the next lower homolog as demonstrated by the cyclization of 5-(2′-naphthyl)pentan-3-one (VIc) to 1-ethyl-3H-benz[e]indene (VII).

It has been reported recently[2] that the polyphosphoric acid cyclization of 6-(2′-naphthyl)-3-hexanone (Ic) followed by dehydrogenation yielded the linear product 1-ethylanthracene (IIc) rather than 4-ethylphenanthrene (IIIc). This unexpected result was ascribed to the well known steric interference between the substituents in the 4 and 5 positions of the phenanthrene system.[3] In order to confirm this supposition and to eliminate the possibility that the cyclization agent played a role, it was decided to examine the scope of this steric effect by altering the size of the ketonic side chain.

Cyclization of 2-β-(2′-naphthyl)-ethylcyclohexanone (Id)[4] followed by dehydrogenation furnished the linear product, benz[*a*]anthracene (IV) and no benzo[*c*]phenanthrene (V) could be detected by ultraviolet examination of the mother liquors. On the other hand, similar treatment of 5-(2-naphthyl)pentan-2-one (Ib), prepared from γ-(2-naphthyl)butyryl chloride and dimethyl cadmium, yielded a mixture of 1-methylanthracene (IIb) and 4-methylphenanthrene (IIIb). The former could be isolated directly in crystalline form while the presence of 4-methylphenanthrene was demonstrated by oxidation of the crude reaction mixture and isolation of 6-methyldiphenic acid.

(1) Monsanto Predoctorate Research Fellow 1954–1956. Present address, Norwich Pharmacal Company, Norwich, N. Y.

(2) H. Bendas and C. Djerassi, *J. Am. Chem. Soc.*, **78**, 2474 (1956).

(3) *Cf.* M. S. Newman, *J. Am. Chem. Soc.*, **62**, 2295 (1940) and later papers.

(4) This ketone was prepared by the Stork reaction [G. Stork, R. Terrell, and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954)] using cyclohexanone pyrrolidine enamine or by alkylation of 2-ethoxycarbonylcyclohexanone.