Substituted 1,10-Phenanthrolines. XIII. The Synthesis of New 4-Mono- and 4,7-Dialkyl- and -aryl-1,10-phenanthrolines[1]

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The synthesis of the following 4-monosubstituted and 4,7-disubstituted 1,10-phenanthrolines is reported: *n*-amyl, cyclohexyl, *p*-tolyl, *p*-ethylphenyl, *p*-*t*-butylphenyl, *p*-biphenylyl; also, 4,7-di-*n*-propyl, -di-*n*-tridecyl, and di-*p*-methoxyphenyl.

Among the many substituted 1,10-phenanthrolines which have been produced in the last decade[2] and tested with regard to their sensitivity as reagents for the detection of iron(II) those containing alkyl or aryl groups in the 4- and/or 7-positions have proved to be the most effective.[3] Thus, in the case of the iron(II) complex of 4,7-diphenyl-1,10-phenanthroline the molecular extinction coefficient is twice that of the parent compound.[4] The object of the present work has been the preparation of new members of this series containing alkyl and aryl radicals of higher molecular weight than those previously prepared.

These compounds were synthesized by first treating *o*-nitroaniline with a β-chloroethyl aryl or alkyl ketone under the conditions of the Yale modification[5] of the Skraup reaction, to form a 4-substituted 8-nitroquinoline. The nitro group was then reduced, and a second Skraup reaction (with the same ketone) converted the resulting amine to the corresponding 4,7-disubstituted 1,10-phenanthroline. The 4-monosubstituted 1,10-phenanthrolines were produced by the reaction of 8-aminoquinoline with the appropriate ketone under the same conditions. The necessary β-chloroethyl alkyl ketones were prepared by the action of an acid chloride on ethene in the presence of aluminum chloride.[6,7] The corresponding aryl ketones resulted from the Friedel-Crafts reaction of β-chloropropionyl chloride and the appropriate aromatic compound.[8]

In the syntheses of the *p*-*t*-butylphenyl-1,10-phenanthrolines, the vinyl ketone was used in the Skraup reaction since the β-chloroethyl ketone originally formed readily lost hydrogen chloride on distillation. The second component used for the preparation of the cyclohexylphenanthrolines was a mixture of cyclohexyl vinyl and β-chloroethyl ketones which resulted on distillation of the reaction product from ethene and hexahydrobenzoyl chloride.

The synthesis of 4,7-bis(2′,4′-dimethylphenyl)-1,10-phenanthroline was attempted. However, because of low yields, only the 8-nitroquinoline derivative was obtained. This was prepared from *o*-nitroaniline and 2,4-dimethyl-β-chloropropiophenone[8] under Yale conditions in only 4% yield.

The synthesis of 4,7-dimesityl-1,10-phenanthroline did not materialize because the intermediate 4-mesityl-8-nitroquinoline could not be prepared from *o*-nitroaniline and vinyl mesityl ketone. By using these reactants under Doebner-Miller conditions, a compound was isolated which is believed to be β-(*o*-nitroanilino)ethyl mesityl ketone. This belief is supported by elemental analysis and infrared data.

Attempts to cyclize this compound failed to produce the desired 4-mesityl-8-nitroquinoline.

Experimental

Reagent for Cyclohexyl Phenanthrolines.—This reagent was prepared from hexahydrobenzoyl chloride and ethene using a method similar to that described by Archer.[6] Upon distilling the crude β-chloroethyl ketone hydrogen chloride split off, and the resulting ketone mixture distilled at 100–110° (3 mm.). This product contained 8.9% chlorine. The calculated value for cyclohexyl β-chloroethyl ketone is 20.9%.

***p*-*t*-Butylphenyl Vinyl Ketone.**—A solution of 1 mole of β-chloropropionyl chloride and 1.05 moles of *t*-butylbenzene was added slowly to 1.05 moles of anhydrous aluminum chloride suspended in 300 ml. of carbon disulfide. After the addition was complete, the reaction mixture was refluxed with stirring for 1 hr., then poured into a mixture of 100 ml. concd. hydrochloric acid and crushed ice. The organic layer was separated, washed three times with water, and dried over anhydrous calcium chloride. The dark liquid residue which remained after removal of the solvent decomposed rapidly upon attempted distillation *in vacuo*. For this reason the crude ketone was used in subsequent Skraup reactions without further purification. The semicarbazone (m.p. 213–213.5°) obtained from this crude product gave a correct analysis for the vinyl derivative.

Anal.: Calcd. for $C_{14}H_{19}N_3O$: C, 68.54; H, 7.81. Found: C, 68.47; H, 7.81.

The Preparation of 4-Substituted 8-Nitroquinolines.—A mixture of 0.2 mole of *o*-nitroaniline, 0.4 mole of arsenic acid, and 200 ml. of 85% phosphoric acid was placed in a 500-ml. Soxhlet flask equipped with a mechanical stirrer and thermometer. The temperature was raised to 100°,

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(2) F. H. Case, "A Review of Syntheses of Organic Compounds Containing the Ferroin Group," G. F. Smith Chemical Co., Columbus, Ohio (1960).

(3) G. F. Smith, *Anal. Chem.*, **26**, 1534 (1954).

(4) D. H. Wilkins, A. A. Schilt, and G. F. Smith, *Anal. Chem.*, **27**, 1574 (1955).

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

(6) S. Archer, U. S. Patent 2,763,662; *Chem. Abstr.*, **51**, 4439 (1957).

(7) H. P. Kaufman and W. Stamm, *Ber.*, **91**, 2121 (1958).

(8) T. Kenner and F. S. Statham, *Ber.*, **69**, 16 (1936); *J. Chem. Soc.*, 299 (1935).

TABLE I

8-NITROQUINOLINES

Substituted 8-Nitroquinoline	Second Component	M.P.	Yield, %	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
4-*n*-Amyl-[a]	1-Chloro-3-octanone[b]	83–84	50	68.83	68.93	6.60	6.42
4-*n*-Tridecyl-[a]	1-Chloro-3-hexadecanone[c]	61.5–62	62	74.10	74.11	9.05	9.04
4-Cyclohexyl-[a]	Vinyl cyclohexyl ketone	157–158	57	70.30	70.66	6.29	6.27
4-*p*-Tolyl-[a]	*p*-Methyl-β-chloropropiophenone[d]	123–124	55	72.73	72.71	4.59	4.84
4-*p*-Ethylphenyl-[a]	*p*-Ethyl-β-chloropropiophenone[d]	71–72	39	73.37	72.98	5.07	5.31
4-*p*-(*t*-Butylphenyl)-[a]	*p*-*t*-Butylphenyl vinyl ketone	167–168	55	74.49	74.54	5.92	5.78
4-*p*-Biphenylyl-[e]	*p*-Phenyl-β-chloropropiophenone[d]	206–207	50	77.28	77.18	4.32	4.54
4-*p*-Methoxyphenyl[f]	*p*-Methoxy-β-chloropropiophenone[g]	134–135	32	68.57	68.67	4.29	4.59

[a] Crystallized from petroleum ether. [b] See ref. 6. [c] See ref. 7. [d] See ref. 8. [e] Crystallized from benzene. [f] Crystallized from methanol, after preliminary extraction with petroleum ether (b.p. 90–100). [g] See ref. 9.

TABLE II

8-AMINOQUINOLINES

8-Aminoquinoline	M.P.	Yield, %	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
4-*n*-Amyl-[a]	53–54	53	78.46	78.71	8.46	8.32
4-*n*-Tridecyl-[a]	66–67	92	80.92	80.70	10.49	10.36
4-Cyclohexyl-[a]	78–79	94	79.62	79.21	8.01	8.14
4-*p*-Tolyl-[a]	107–108	65	82.02	82.11	6.02	6.12
4-*p*-Ethylphenyl-[a]	81–82	65	82.22	81.97	6.49	6.34
4-*p*-Biphenylyl-[b]	165–166	77	85.10	85.04	5.44	5.51
4-*p*-Methoxyphenyl-[c]	148–149	96	76.80	77.12	5.60	5.46

[a] Crystallized from petroleum ether. [b] Crystallized from benzene–petroleum ether. [c] Crystallized from benzene.

TABLE III

1,10-PHENANTHROLINES

1,10-Phenanthroline	1st Component quinoline	2nd Component	M.P.	Yield, %	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
4,7-Di-*n*-propyl-[a]	4-*n*-Propyl-8-amino-	1-Chloro-3-hexanone[b]	59–60	10	81.82	81.92	7.58	7.78
4-*n*-Amyl-[a]	8-Amino-	1-Chloro-3-octanone[b]	91–92	6	81.56	81.91	7.24	7.02
4,7-Di-*n*-amyl-[a]	4-*n*-Amyl-8-amino-	1-Chloro-3-octanone	56–57	51	82.45	82.18	8.86	8.75
4,7-Bis(*n*-tridecyl)-[a]	4-*n*-Tridecyl-8-amino-	1-Chloro-3-hexadecanone[c]	78–79	40	83.76	83.95	11.10	11.03
4-Cyclohexyl-[d]	8-Amino-	Vinyl cyclohexyl ketone	163–164	17	82.40	82.42	6.92	7.05
4,7-Dicyclohexyl-[a]	4-Cyclohexyl-8-amino-	Vinyl cyclohexyl ketone	168–169	21	83.67	83.75	8.19	8.27
4-*p*-Tolyl-[d]	8-Amino-	*p*-Methyl-β-chloropropiophenone	169–170	13	84.42	84.27	5.22	5.22
4,7-Di(*p*-tolyl)-[a]	4-(*p*-tolyl)-8-amino-	*p*-Methyl-β-chloropropiophenone	184–185	15	86.63	86.49	5.59	5.90
4-(*p*-Ethylphenyl)-[a]	8-Amino-	*p*-Ethyl-β-chloropropiophenone	151–152	18	84.48	84.73	5.67	5.78
4,7-Bis(*p*-ethylphenyl)-[a]	4-*p*-Ethylphenyl-8-amino-	*p*-Ethyl-β-chloropropiophenone	138–139	3	86.56	86.62	6.23	5.87
4-*p*-(*t*-Butylphenyl)-[a]	8-Amino-	*p*-*t*-Butyl-β-chloropropiophenone	171–172	15	84.58	84.66	6.45	6.52
4,7-Bis(*t*-butylphenyl)-[e]	4-*p*-*t*-Butylphenyl-8-amino-	*p*-*t*-Butyl-β-chloropropiophenone	295–296	9	86.44	86.31	7.25	7.13
4-*p*-Biphenylyl-[d]	8-Amino-	*p*-Phenyl-β-chloropropiophenone	192.5–193.5	30	86.74	86.89	4.85	4.77
4,7-Bis(*p*-biphenylyl)-[f]	4-*p*-Biphenylyl-8-amino-	*p*-Phenyl-β-chloropropiophenone	291–292	47	89.23	89.06	4.99	5.12
4,7-Bis-*p*-methoxyphenyl-[f]	4-*p*-Methoxyphenyl-8-amino-	*p*-Methoxy-β-chloropropiophenone	208–209	33[g]	79.57	79.55	5.10	5.31

[a] Crystallized from petroleum ether. [b] See ref. 6. [c] See ref. 7. [d] Crystallized from benzene–petroleum ether. [e] Crystallized from ethanol–water. Product isolated as monohydrate. [f] Crystallized from benzene. [g] Based on material melting at 204°.

and 0.3 mole of ketone was added at such a rate that the temperature did not exceed 120°. After the addition of the ketone was complete, the temperature was maintained at 120–130° for 1 hr., then raised slowly to 140° over a period of 0 5 hr. The total reaction time should never be allowed to exceed two hours. After cooling, the reaction mixture was poured on ice and made alkaline with potassium hydroxide. The (usually tarry) residue was filtered from the solution, and both the solution and the residue were extracted with hot benzene. The benzene was removed by distillation, and the residue was crystallized from a suitable solvent (Table I).

The Preparation of 4-Substituted 8-Aminoquinolines.—To a solution of 1.5 moles of stannous chloride dihydrate in 700 ml. of absolute ethanol was added 0.5 mole of the 4-substituted 8-nitroquinoline. The mixture was refluxed on a steam bath for 4 hr., after which most of the ethanol was removed by distillation. The residual solution was made alkaline with sodium hydroxide and filtered. Both the filtrate and the residue were extracted with ether, and the combined ether extracts were dried over anhydrous sodium sulfate. After removal of the solvent, the residue was crystallized from a suitable solvent (Table II).

General Procedure for the Synthesis of 1,10-Phenanthrolines.—To a well stirred solution of 0.05 mole of the appropriate amine, 0.1 mole of arsenic acid, and 50 ml. of 85% phosphoric acid heated to 100° was added 0.07 mole of the appropriate ketone at such a rate that the temperature did not exceed 120°. When the addition of the ketone was complete, the temperature was raised slowly to 140°, and maintained there for 1 hr. The reaction mixture was then cooled, poured on ice, made alkaline with a solution of concd. potassium hydroxide, and the precipitate which formed was extracted with hot benzene. After removal of the solvent, the residue was purified by crystallizing from a suitable solvent (Table III).

In the case of 4,7-bis(*p*-ethylphenyl)-1,10-phenanthroline, the crude residue was purified by precipitating the hydrochloride from the benzene solution, making alkaline, and then proceeding as before.

β-(*o*-Nitroanilino)ethyl Mesityl Ketone.—Twenty-six grams (0.13 mole) of vinyl mesityl ketone was added slowly to a well stirred solution of 13.8 g. (0.1 mole) of *o*-nitroaniline, 11.5 g. (0.08 mole) of arsenic acid, 10 g. (0.07 mole) of anhydrous zinc chloride, and 200 ml. of concd. hydrochloric acid heated on a steam bath. After the addition of the ketone was complete, the mixture was refluxed for 3 hr., then poured on ice, and finally made alkaline with potassium hydroxide. The resulting precipitate was removed by filtration, dried, and extracted with hot benzene. Removal of benzene and crystallization from petroleum ether yielded 20 g. of product which melted at 100–101°. Infrared absorption bands were found at 2.96, 6.35, 11.59, 13.33 μ.

Anal. Calcd. for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.46; N, 8.94. Found: C, 69.61; H, 6.46; N, 8.88.

(9) E. Profft, F. Runge, and A. Jumar, *J. prakt. Chem.* [4], **1**, 57 (1954).

Some Aspects of the Chemistry of the Bicyclo[5.4.0]undecane Ring System. Synthesis of Several Tetrahydrobenzosuberones[1]

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The synthesis of bicyclo[5.4.0]undec-4-en-5-one and bicyclo[5.4.0]undec-10-en-5-one by the polyphosphoric acid cyclization of 5-(1′-cyclohexenyl)valeric acid is described. The ultraviolet spectral properties and other physical properties were found to be identical in all respects with the properties reported for the products of the selenium dioxide dehydrogenation of *cis*- and *trans*-bicyclo[5.4.0]undecan-5-one. The selenium dioxide dehydrogenation reaction and structural assignments are re-interpreted in light of this study.

Recently, Ginsberg and Rosenfelder[2] reported the formation of several bicyclo[5.4.0]undecenones (tetrahydrobenzosuberones) by the selenium dioxide dehydrogenation of *cis*- and *trans*-bicyclo[5.4.0]undecan-5-one (I and II, respectively, Fig. 1). The assignment of the position of the olefinic linkage in the dehydrogenated species was based upon the ultraviolet spectral characteristics of the α,β-unsaturated ketones and their derivatives as well as upon the further reactivity of these products with *N*-bromosuccinimide followed by treatment with lutidine to form doubly unsaturated ketones. The selenium dioxide dehydrogenation of *cis*-bicyclo[5.4.0]undecan-5-one (I) was presumed to take place at C-6 rather than at the ring junction, tertiary carbon, C-11 adjacent to the carbonyl group to yield *cis*-bicyclo[5.4.0]undec-6-en-5-one (III). It was reasoned that the molecular geometry of the *cis* ring system does not permit attack of the reagent at the ring junction. However, treatment of the *trans* ketone (II) in a like manner yielded bicyclo[5.4.0]undec-10-en-5-one (IV). In the latter reaction, attack of the reagent undoubtedly took place at the ring junction.

It was surprising indeed that the attack of selenium dioxide took place in the *cis* ring system at a position other than at the tertiary carbon at the ring junction. Although Mel'nikov and Rokitskaya[3] have postulated the initial reaction of selenium dioxide is through the formation of the enol ester, it was later proposed by Duke[4] that the

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(2) D. Ginsberg and W. J. Rosenfelder, *Tetrahedron*, **1**, 3 (1957).

(3) N. N. Mel'nikov and M. S. Rokitskaya, *J. Gen. Chem.* (*U.S.S.R.*), **7**, 2738 (1937).

(4) F. R. Duke, *J. Am. Chem. Soc.*, **70**, 419 (1948).