[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

Substituted 1,10-Phenanthrolines. IX. Cycloalkeno Derivatives[1]

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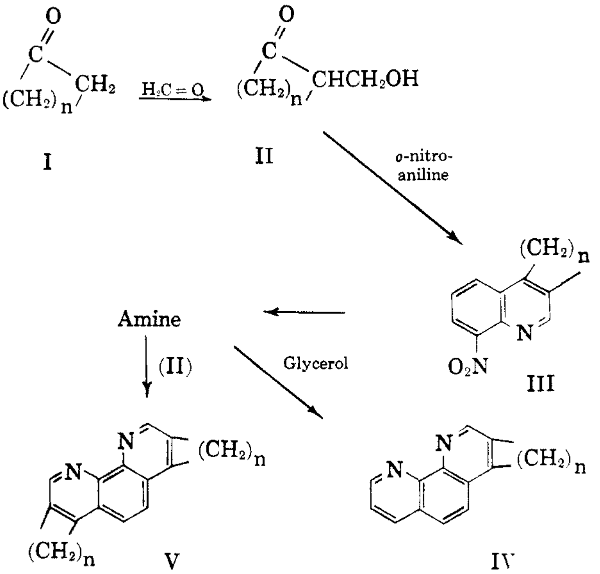
2-Hydroxymethyl derivatives of cyclopentanone, cycloheptanone, and cyclooctanone have been prepared. *o*-Nitroaniline has been caused to react in a modified Skraup reaction with 2-hydroxymethylcyclo-pentanone, -hexanone, -heptanone, and -octanone.

Four 3,4-cycloalkeno- and three 3,4,7,8-dicycloalkeno-1,10-phenanthrolines have been prepared and the preparation of 3,4-benzo-1,10-phenanthroline is described.

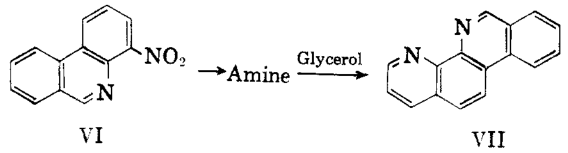
By the action of formalin on cyclohexanone Kenner, Ritchie, and Statham[2] obtained 2-hydroxymethylcyclohexanone, which was condensed with aniline in a Doebner-von Miller reaction to form 1,2,3,4-tetrahydrophenanthridine. Dehydrogenation with selenium then yielded phenanthridine. These authors, however, were unable to bring about a similar condensation of formalin and cyclopentanone.

In this laboratory the condensation of formalin with cyclopentanone, cycloheptanone, and cyclooctanone (I; n = 3,5,6) has been accomplished. It has been found that the aforementioned four hydroxymethylcycloalkanones (II; n = 3,4,5,6) (which were not purified) react with *o*-nitroaniline in a modified Skraup reaction[3] to yield the corresponding 3,4-cycloalkeno-8-nitroquinolines (III). With aniline the reaction is for the most part unsatisfactory. From the corresponding amino derivatives, 3,4-mono- (IV) and 3,4,7,8-dicycloalkeno-1,10-phenanthrolines (V) were prepared.

Attempts to dehydrogenate IV and V (n = 4) to the corresponding 3,4-benzo- and 3,4,7,8-dibenzo-1,10-phenanthrolines were unsuccessful. However, dehydrogenation of [III (n = 4)] by means of chloranil yielded 4-nitrophenanthridine (VI), previously prepared by Caldwell and Walls[4] by decarboxylation of 4-nitrophenanthridine-6-carboxylic acid. Reduction, followed by a Skraup reaction, yielded 3,4-benzo-1,10-phenanthroline (VII). The molecular extinction coefficients of the Cu^+ and Fe^{++} complexes of the substituted phenanthrolines described above will be determined.



In formulas I–IV, n = 3,4,5, and 6.
In formula V, n = 3,4, and 5.



EXPERIMENTAL PART[5]

2-Hydroxymethylcyclopentanone. (The procedure was essentially that of Kenner, Ritchie, and Statham[2] as applied to cyclohexanone). To a stirred mixture of 84 g. of cyclopentanone, 10 ml. of water, and 65 g. of 37% formalin solution, 1 g. of calcium hydroxide was added at such a rate that the temperature did not rise above 40°. After standing overnight two such runs were combined, acidified with dilute acetic acid, saturated with ammonium sulfate, and extracted with ether. The solution was dried over sodium sulfate, the ether was removed, and the residue was distilled *in vacuo*. The yield of crude product boiling at 100–120° (8 mm.) was 19.3 g. From the lower-boiling fraction, 59.6 g. of unchanged cyclopentanone (b.p. 125–132°) was recovered. The yield, allowing for the unchanged cyclopentanone, was 13.1%.

By warming the hydroxymethylcyclopentanone with phenyl isocyanate and crystallizing from petroleum ether, the *phenylurethan* was obtained, m.p. 89–90°.

Anal. Calc'd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48. Found: C, 67.12; H, 6.66.

2-Hydroxymethylcycloheptanone. Starting with 110 g. of cycloheptanone, 10 ml. of water, 72 g. of 37% formalin solution, and 1.2 g. of calcium hydroxide the previous procedure was attempted. However, since no spontaneous warming was observed the mixture was maintained at 50° for 6 hours and then was worked up as before. Fractional distillation yielded 52 g. of a liquid boiling at 132–160° (23 mm.). The lower-boiling portion afforded 36 g. of unchanged cyclo-

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

[2] Kenner, Ritchie, and Statham, *J. Chem. Soc.*, 1169 (1937).

[3] Yale and Bernstein, *J. Am. Chem. Soc.*, **70**, 254 (1948).

[4] Caldwell and Walls, *J. Chem. Soc.*, 2156 (1952).

[5] Analyses were done by Huffman Microanalytical Laboratories, Wheatridge, Colorado.

heptanone, b.p. 174–182°. The yield of crude product, allowing for the unchanged ketone, was 55.4%. The *phenylurethan*, crystallized from petroleum ether, melted at 89–90°.

Anal. Calc'd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33. Found: C, 69.13; H, 7.34.

2-Hydroxymethylcycloöctanone. The previous procedure was applied to a mixture of 98 g. of cycloöctanone, 10 ml. of water, 60 g. of 37% formalin solution, and 1 g. of calcium hydroxide heated to 40–45°. Distillation yielded 50 g. of a fraction, b.p. 163–183° (22 mm.) plus 37 g. of recovered cycloöctanone, b.p. 190–208°. The yield, allowing for recovered ketone, was 66.2%.

The *phenylurethan*, crystallized from petroleum ether, melted at 98–99°.

Anal. Calc'd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69. Found: C, 69.89; H, 7.62.

Synthesis of 3,4-cycloalkeno-8-nitroquinolines. A stirred mixture of 13.8 g. (0.1 mole) of *o*-nitroaniline, 24 g. of arsenic acid, and 100 ml. of 85% phosphoric acid was heated to 100° and treated with 0.12 mole of 2-hydroxymethylcycloalkanone (0.2 mole in the case of hydroxymethylcyclohexanone) keeping the temperature below 120°. After two hours' heating at this temperature, the reaction mixture was poured into ice-water, neutralized with potassium hydroxide solution, and the precipitate was removed by filtration. Extraction of the precipitate with benzene, removal of solvent, and crystallization from benzene (methanol in the case of 3,4-cycloöcteno-8-nitroquinoline) yielded the pure 3,4-cycloalkeno-8-nitroquinoline.

3,4-Cyclopentenoquinoline. The procedure for the synthesis of 3,4-cycloalkeno-8-nitroquinolines was applied to a mixture of 14 g. of aniline, 36 g. of arsenic acid, 150 ml. of 85% phosphoric acid, and 24 g. of 2-hydroxymethylcyclopentanone. After the reaction mixture had been made alkaline. it was extracted with warm benzene. The oily residue remaining after evaporation of the benzene was extracted with petroleum ether (b.p. 90–100°). The residue, after removal of this solvent, still an oil, was converted to the *picrate*, of which 1.7 g. was obtained after crystallization from acetone. It melted at 216–217° (dec.). No attempt was made to liberate the base from this small amount of picrate.

Anal. Calc'd for $C_{18}H_{14}N_4O_7$: C, 54.27; H, 3.54. Found: C, 54.56; H, 3.77.

3,4-Cycloheptenoquinoline. Using the previous procedure, with exactly the same amounts of aniline, arsenic acid, and phosphoric acid and 24 g. of 2-hydroxymethylcycloheptanone, 9 g. of an oil was obtained after removal of petroleum ether. Conversion to the *picrate* yielded 5.7 g., melting at 193–194° after crystallization from acetone.

Anal. Calc'd for $C_{20}H_{18}N_4O_7$: C, 56.33; H, 4.26. Found: C, 56.65; H, 4.49.

By refluxing the picrate with dilute hydrochloric acid and benzene, repeated extraction with benzene, and making the aqueous layer alkaline, the *pure base* was obtained. After crystallization from petroleum ether it melted at 67–68°.

Anal. Calc'd for $C_{14}H_{15}N$: C, 85.22; H, 7.66. Found: C, 85.19; H, 7.64.

From the mixture obtained by the action of hydroxymethylcycloöctanone on aniline no picrate could be obtained.

4-Nitrophenanthridine. A mixture of 8.3 g. of 4-nitro-7,8,9,-10-tetrahydrophenanthridine [III (n = 4)], 18.8 g. of chloranil, and 140 ml. of xylene was refluxed with stirring for 10 hours. The hot solution then was filtered from the chlorohydroquinone, the filtrate was washed thoroughly with 7% potassium hydroxide solution, and the solvent was evaporated *in vacuo*. The residue, on crystallization from benzene, yielded 3.3 g. of a substance melting at 187–188°. (Caldwell and Walls[4] report m.p. 191–192°, with shrinking at 187°.)

Anal. Calc'd for $C_{13}H_8N_2O_2$: C, 69.64; H, 3.60. Found: C, 69.88; H, 3.50.

4-Aminophenanthridine. This substance was prepared from the corresponding nitro compound by the method of Elderfield[6] (stannous chloride and hydrochloric acid). After crystallization from benzene-petroleum ether it melted at 125–126°.

Anal. Calc'd for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19. Found: C, 80.02; H, 5.28.

TABLE I

3,4-CYCLOALKENO-8-NITROQUINOLINES

				Analyses			
			Molecular	Carbon		Hydrogen	
Substituent	M.p., °C.	Yield, %	formula	Calc'd	Found	Calc'd	Found
Cyclopenteno-	131–132	15.4	$C_{12}H_{10}N_2O_2$	67.28	67.24	4.71	4.53
Cyclohexeno-	143–144	24.0	$C_{13}H_{12}N_2O_2$	68.42	68.44	5.26	5.24
Cyclohepteno-	132–133	31.1	$C_{14}H_{14}N_2O_2$	69.40	69.68	5.82	5.73
Cycloöcteno-	143–144	7.8	$C_{15}H_{16}N_2O_2$	70.29	70.27	6.29	6.15

TABLE II

3,4-CYCLOALKENO-8-AMINOQUINOLINES

				Analyses			
		Crystallizing	Molecular	Carbon		Hydrogen	
Substituent	M.P., °C.	solvent	formula	Calc'd	Found	Calc'd	Found
Cyclopenteno-	117–118	Methanol	$C_{12}H_{12}N_2$	78.22	77.90	6.57	6.66
Cyclohexeno-	105–106	Methanol	$C_{13}H_{14}N_2$	78.74	78.47	7.12	7.23
Cyclohepteno-	120–121	Benzene	$C_{14}H_{16}N_2$	79.21	79.44	7.60	7.65
Cycloöcteno-	107–108	Petroleum ether	$C_{15}H_{18}N_2$	79.60	79.93	8.02	8.07

8-Amino-3,4-cycloalkenoquinolines. With the exception of 3,4-cycloöcteno-8-nitroquinoline, which was reduced catalytically, the cycloalkeno-8-nitroquinolines were reduced by stannous chloride in hydrochloric acid.[6]

Preparation of 3,4-cycloalkeno-1,10-phenanthrolines. A mixture of one molar proportion of the appropriate aminoquinoline, one mole of arsenic acid hemihydrate, ten moles of sulfuric acid in 96.8% solution, and a volume of water equal to one-third of the volume of sulfuric acid used was heated to 100° and treated with glycerol (5 moles) at such a rate that the temperature did not exceed 140°. Heating was continued at this temperature for two hours. The mixture then was poured into water, made alkaline with sodium hydroxide, and the precipitate was removed by filtration.

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(6) Elderfield, *et al.*, *J Am. Chem. Soc.*, **68**, 1586 (1946).

TABLE III

3,4-CYCLOALKENO-1,10-PHENANTHROLINES

				Analyses			
			Molecular	Carbon		Hydrogen	
Substituent	Yield, %	M.p., °C.	formula	Calc'd	Found	Calc'd	Found
Cyclopenteno-	17.5	207–208	$C_{15}H_{12}N_2$	81.79	81.91	5.49	5.61
Cyclohexeno-	34.7	208–209	$C_{16}H_{14}N_2$	82.01	81.90	6.03	5.98
Cyclohepteno-	35.8	164–165	$C_{17}H_{16}N_2$	82.22	82.51	6.50	6.65
Cycloöcteno-	42.5	145–146	$C_{18}H_{18}N_2$	82.41	82.58	6.92	6.92

TABLE IV

3,4,7,8-DICYCLOALKENO-1,10-PHENANTHROLINES

				Analyses			
			Molecular	Carbon		Hydrogen	
Substituent	Yield, %	M.p., °C.	formula	Calc'd	Found	Calc'd	Found
Dicyclopenteno-	10.0	282–283	$C_{18}H_{16}N_2$	83.04	83.37	6.20	6.28
Dicyclohexeno-	24.5	259–260	$C_{20}H_{20}N_2$	83.33	83.17	6.94	7.02
Dicyclohepteno-	17.3	256–257	$C_{22}H_{24}N_2$	83.50	83.64	7.65	7.71

The filtrate was extracted three times with benzene, which then was used to extract the phenanthroline from the solid material. After removal of solvent the phenanthroline was crystallized from benzene.

3,4-Benzo-1,10-phenanthroline. This substance was prepared by a Skraup reaction on 4-aminophenanthridine similar to those used for the preparation of 3,4-cycloalkeno-1,10-phenanthrolines. The yield of product crystallizing from benzene-petroleum ether, and melting at 157–158° was 11%.

Anal. Calc'd for $C_{16}H_{10}N_2$: C, 83.45; H, 4.38. Found: C, 83.27; H, 4.51.

Preparation of 3,4,7,8-dicycloalkeno-1,10-phenanthrolines. A stirred mixture of one molar proportion of 8-amino-3,4-cycloalkenoquinoline, one mole of arsenic acid hemihydrate, and 20 moles of phosphoric acid in 85% solution was heated to 100° and treated with 1.8 moles of 2-hydroxymethylcycloalkanone at such a rate that the temperature did not rise above 120°. After two hours at this temperature the reaction mixture was poured on ice, neutralized with a potassium hydroxide solution, and the precipitate was removed by filtration. The filtrate was extracted three times with warm benzene, which then was used to extract the phenanthroline from the solid material. After removal of the solvent the phenanthroline was crystallized from benzene.

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