

HETEROCYCLIC ANALOGS OF PLEIADIENE.

53.* PROPERTIES OF 1,9-TRIMETHYLENEPERIMIDENE

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The behavior of 1,9-trimethyleneperimidine (3,4,5,6-tetrahydropyrido[3,2,1-k,7]-perimidine) with respect to nucleophilic agents was studied. It is shown that the properties of 1,9-trimethyleneperimidine are virtually the same as the properties of 1-alkylperimidines.

3,4,5,6-Tetrahydropyrido[3,2,1-k,7]perimidine (or 1,9-trimethyleneperimidine) (I), which we recently synthesized [1], is actually the first representative of difficult-to-obtain 1,9-disubstituted perimidines. It therefore seemed of interest to study some properties of this compound. In the present paper we describe the behavior of I and its quaternary salts with respect to nucleophilic agents, as well as a number of other reactions.

Compound I, like 1-substituted perimidines [2, 3], readily undergoes amination by sodium amide or hydroxylation by fused alkali, as a result of which amine II and perimidone III, respectively, are formed in high yields. Methiodide IV, which was obtained by the action of methyl iodide on I, under the influence of aqueous alkali undergoes disproportionation to give perimidone V and 2,3-dihydropyrimidine VI in 44 and 38% yields, respectively. The certain preponderance of the perimidone structure in this reaction is also characteristic for 1,3-dialkylperimidinium salts [4].

We also accomplished the recyclization of I, which makes it possible to introduce a phenyl group in the 2 position. Compound VII was obtained in 85% yield.

The synthesis of perimidone III made it possible to build on yet another trimethylene bridge in the 1 and 4 positions. Compound III was subjected to cyanoethylation with acrylonitrile in xylene in the presence of sodium amide. Cyanoethyl derivative IX was obtained in 38% yield. When IX is refluxed in concentrated HCl, it is converted to intramolecular acylation product X in 60% yield. Dioxo derivative X was converted via the Wolff-Kishner reaction to new heterocyclic system XI, the synthesis of which from 1,3-bis(β -cyanoethyl)-perimidone could not be accomplished [1]. The structures of all of the synthesized compounds were confirmed by data from IR and PMR spectroscopy and the results of elementary analysis.

Thus, with respect to nucleophiles, 1,9-trimethyleneperimidine differs little from 1-alkylperimidines.

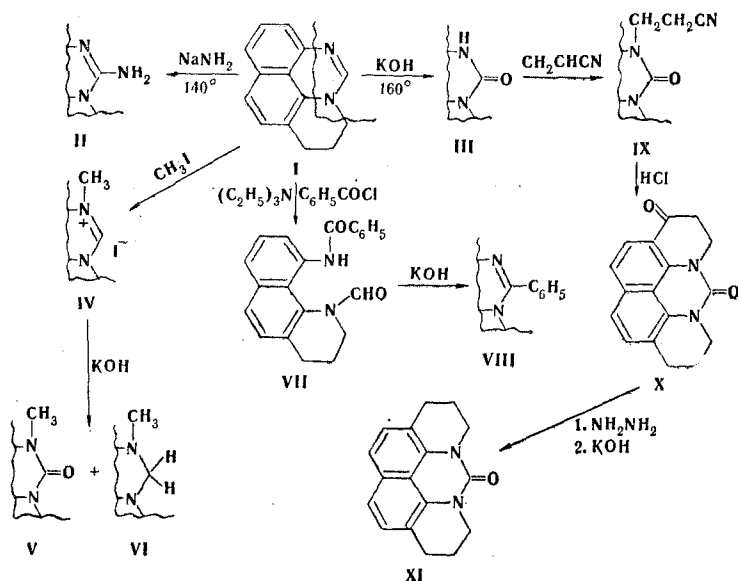
EXPERIMENTAL

The IR spectra were measured with a UR-20 spectrometer, while the PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. Chromatography was carried out on aluminum oxide.

2-Amino-3,4,5,6-tetrahydropyrido[3,2,1-k,7]perimidine (II). A mixture of 0.6 g (3 mmole) of I and 0.35 g (9 mmole) of sodium amide in 3 ml of absolute dimethylaniline was stirred at 140°C for 1-1.5 h in a nitrogen atmosphere, during which a precipitate formed. The mixture was then cooled and treated with 2 ml of water while a strong stream of nitrogen was passed through it. The precipitate was removed by filtration and washed with water,

*See [1] for communication 52.

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benzene, and petroleum ether to give 0.52 g (80%) of white crystals with mp 177-178°C (dec., from dioxane). IR spectrum (mineral oil): 3400, 3200, and 1688 cm^{-1} (NH_2). Found: C 75.2; H 5.6; N 18.9%. $\text{C}_{14}\text{H}_{13}\text{N}_3$. Calculated: C 75.3; H 5.8; N 18.8%.

2-Oxo-3,4,5,6-tetrahydropyrido[3,2,1-k,7]perimidine (III). A mixture of 2.28 g (11 mmole) of I and 2.8 g (50 mmole) of finely ground fused KOH was heated to 160°C and maintained at this temperature for 1 h. It was then treated with 40 ml of 5% aqueous HCl solution until it was acidic with respect to Congo Red, and the resulting precipitate was removed by filtration to give 1.44 g (60%) of white crystals with mp 250-251°C (from xylene). IR spectrum (CHCl_3): 3430 (NH) and 1680 cm^{-1} ($\text{C}=\text{O}$). Found: C 74.7; H 5.4; N 12.5%. $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}$. Calculated: C 75.0; H 5.3; N 12.5%.

3,4,5,6-Tetrahydropyrido[3,2,1-k,7]perimidine Methiodide (IV). A mixture of 0.8 g (4 mmole) of I and 0.4 ml (6 mmole) of methyl iodide in 5 ml of absolute benzene was refluxed for 30 min, after which it was cooled, and the resulting precipitate was removed by filtration to give 1.1 g (84%) of yellow needles with mp 243.5-244.5°C (from alcohol). IR spectrum (mineral oil): 3370 and 3430 cm^{-1} (crystallization water). Found: C 49.9; H 4.8; I 32.3; N 7.8%. $\text{C}_{15}\text{H}_{15}\text{IN}_2 \cdot \frac{1}{2} \text{H}_2\text{O}$. Calculated: C 49.6; H 4.5; I 32.6; N 7.8%.

Action of Alkali on IV. A 30-ml sample of 10% KOH solution was added to a suspension of 3.7 g (10 mmole) of IV in 100 ml of water, and the mixture was allowed to stand on a boiling-water bath for 1 h. The precipitate was removed by filtration and treated with 15% HCl, and the insoluble residue, which was primarily 2-oxo-1-methyl-3,4,5,6-tetrahydropyrido[3,2,1-k,7]perimidine (V), was purified by chromatography (elution with benzene) to give 1.1 g (44%) of white crystals with mp 131-132°C (from octane). With respect to its physicochemical properties, the product was identical to the compound obtained by the method in [1]. The hydrochloric acid filtrate was made alkaline to pH 8 with ammonia, and the resulting precipitate, which was primarily 1-methyl-1,2,3,4,5,6-hexahydropyrido[3,2,1-k,7]perimidine (VI), was removed by filtration and purified by chromatography (elution with benzene) to give 0.9 g (38%) of white crystals with mp 139-140°C (from alcohol). Found: C 80.1; H 6.7; N 12.5%. $\text{C}_{15}\text{H}_{16}\text{N}_2$. Calculated: C 80.4; H 7.0; N 12.5%.

1-Formyl-10-benzamidobenzo[h]-1,2,3,4-tetrahydroquinoline (VII). A 1.1-ml (10 mmole) sample of triethylamine and 1 ml (8.5 mmole) of freshly distilled benzoyl chloride were added with stirring to a solution of 1.7 g (8.2 mmole) of I in 70 ml of ether and 10 ml of benzene, and the mixture was refluxed on a water bath for 1 h. It was then cooled, and the precipitate was removed by filtration and washed with water to give 2.3 g (85%) of white crystals with mp 165-166°C (from toluene or alcohol). IR spectrum (CHCl_3): 3430 (NH) and 1680 cm^{-1} ($\text{C}=\text{O}$). Found: C 76.2; H 5.3; N 8.2%. $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_2$. Calculated: C 76.3; H 5.5; N 8.5%.

2-Phenyl-3,4,5,6-tetrahydropyrido[3,2,1-k,7]perimidine (VIII). A suspension of 1 g (3 mmole) of VII in 40 ml of 10% aqueous KOH solution was refluxed for 2 h, after which it was cooled, and the precipitate was removed by filtration and washed with water to give

0.7 g (81%) of yellow crystals with mp 146-147°C (from alcohol). With respect to its physicochemical characteristics, the product was identical to the compound obtained by the method in [1].

1-β-Cyanoethyl-2-oxo-3,4,5,6-tetrahydropyrido[3,2,1-k,7]perimidine (IX). A 10-ml (150 mmole) sample of acrylonitrile was added dropwise with vigorous stirring to a refluxing suspension of 1.98 g (9 mmole) of III and 0.5 g (15 mmole) of sodium amide in 200 ml of absolute xylene, after which the mixture was refluxed for 3 h. The hot mixture was filtered to remove the polymers, and the filtrate was evaporated *in vacuo* (with a water aspirator). The residue was dissolved in 15 ml of chloroform and passed through a chromatographic column (elution with CHCl₃) with collection of the first fraction, workup of which gave 0.95 g (38%) of white crystals with mp 196-197°C (from alcohol). IR spectrum (CHCl₃): 2260 (C≡N) and 1665 cm⁻¹ (C=O). Found: N 14.7%. C₁₇H₁₅N₃O. Calculated: N 15.1%.

1,5-Dioxo-1,2,3,4,6,7,8,9-octahydrobispyrido[1,2,3-c,d;3',2',1'-k,7]perimidine (X). A solution of 0.4 g (1.4 mmole) of IX in 4 ml of concentrated HCl was refluxed for 3 h, after which it was cooled, and the resulting precipitate was removed by filtration, washed with water, and purified by chromatography (CHCl₃) to give 0.25 g (60%) of yellow-crystals with mp 218.5-219°C (from toluene). PMR spectrum (CF₃COOH): 1.55 (m, 2H, CH₂), 2.37 (m, 4H, 2-CH₂), 3.37 (m, 4H, 2-CH₂), and 6.65 ppm (m, 4H, 5-H-8-H). IR spectrum (CHCl₃): 1670 cm⁻¹ (C=O).

2-Oxo-1,2,3,4,6,7,8,9-octahydrobispyrido[1,2,3-c,d;3',2',1'-k,7]perimidine (XI). A solution of 0.35 g (1.26 mmole) of X and 0.2 ml (4 mmole) of 99% hydrazine hydrate in 10 ml of diethylene glycol was stirred at 120°C for 2 h, after which 0.2 g (3.4 mmole) of finely ground dry KOH was added, and the temperature was raised to 200°C. The mixture was then stirred at this temperature until the excess hydrazine hydrate and water were completely removed by distillation. The mixture was then poured into 50 ml of ice water, and the resulting precipitate was removed by filtration and washed with water to give 0.3 g (81%) of white crystals with mp 171-172°C (from alcohol). Found: N 10.4%. C₁₇H₁₄N₂O. Calculated: N 10.6%. PMR spectrum (in CDCl₃): 1.87 (m, 4H, 2-CH₂), 2.65 (m, 4H, 2-CH₂), 3.85 (m, 4H, 2-CH₂), and 6.95 ppm (s, 5-H-8-H).

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