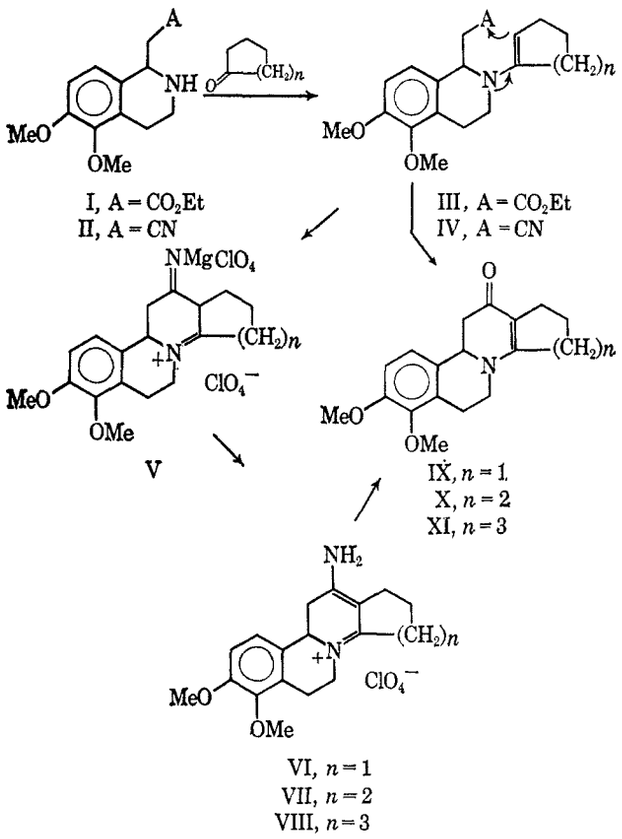
The melting point, on admixture with IX obtained from the above method, was 175–177°.

8-Aza-D-homo-18-norestrone Methyl Ether (I).—A solution of 803 mg of IX (crude material from 1.03 g of VIII) in 40 ml of acetone, cooled to 0°, was treated with 2 ml of Jones reagent over a 10-min period. The mixture was stirred for 15 min and the excess of oxidizing agent was decomposed with sulfur dioxide. The acetone was removed under reduced pressure and the aqueous solution was extracted with chloroform. The extracts were washed with water and dried (sodium sulfate). The residual oil, upon solvent removal, was dissolved in a minimum amount of benzene and passed through 5 g of alumina. Evaporation of the eluent afforded a colorless solid, which upon recrystallization from *n*-hexane gave crystalline product I (343 mg, 44% over-all yield from both steps): mp 143–144° (lit.[3] 143.5–144.0°); λ^{CHCl_3} 3.58, 3.65 (Bohlmann bands[4]), 5.81, 6.17, 6.63 μ; nmr (τ, $CDCl_3$), 2.75–3.35 three protons (aromatic, multiplet), 6.24, three protons (methoxyl, singlet), 6.28–6.40, one proton (multiplet, C-9).

Catalytic Reduction of I to IX.—A solution of 62 mg of I in 5 ml of ethanol containing 20 mg of platinum oxide and 0.05 ml of 70% perchloric acid was hydrogenated for 15 min after which the theoretical quantity of hydrogen was taken up. The solution was shaken with solid potassium carbonate for 30 min and then filtered to obtain a clear ethanolic solution, which was evaporated *in vacuo*. The residual solid was recrystallized from ether–benzene to give 51 mg (82%) of IX, mp 174–176°. The mixture melting point showed no depression. The infrared and nmr spectra were identical with those of IX prepared by reduction of VI or VIII.

Registry No.—V, 7688-14-4; VIII, 7641-74-9; IX, 7641-75-0; I, 7641-76-1.



The Synthesis of 7-Aminobenzo[*a*]cycloalkano[*f*]-quinolizinium Perchlorates. An Example of the Addition of Enamines to the Nitrile Function[1]

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The addition of enamines to electrophilic olefins,[2] acid chlorides,[2] isocyanates,[3] isothiocyanates,[3] and esters[4] is now well known. Only a few reports,[5] however, have been made concerning the direct addition of enamines to the nitrile group. We now wish to describe a facile addition of enamines to the triple bond of a nitrile function utilizing the complexing ability of the magnesium ion. In previous studies[4] from this laboratory, it was shown that the attempted enamine formation using the isoquinoline ester (I) and cyclic ketones (n = 1, 2, and 3) resulted not in the simple enamines (III), but in the tetracyclic enamino ketones (IX–XI). This intramolecular cyclization led to further studies involving enamine additions to other π-electron-containing functional groups. When the isoquinolinenitrile (II), prepared from the corresponding phenylethylamine and ethyl cyanoacetate, was treated with cyclohexanone in refluxing toluene containing a trace of acid, only a small quantity of the enamine (IV) and a 70% recovery of the isoquinoline nitrile were obtained. It, therefore, appeared that the nitrile group is not sufficiently electrophilic to allow cyclization to occur. The fact that magnesium ion forms an effective complex with the imino group (*i.e.*, Grignard reactions involving nitriles) and perchlorate salts of amines are usually quite stable, magnesium perchlorate was considered as a suitable reagent for this cyclization process.[6] When 1 equiv of anhydrous magnesium perchlorate was added to the reaction mixture, there was obtained, after 40 hr of reflux, an amorphous solid (presumably V). Upon removal of the latter from the toluene solution and treatment with aqueous alkali, a 95% yield of the aminoquinolizinium salt (VII) was obtained (Table I). The reaction was repeated, in the same manner, using cyclopentanone and cycloheptanone resulting in somewhat lower yields of the aminoquinolizinium salts. The stability of VI, VII, and VIII to aqueous alkali is surprising; however, iminium salts containing analogous structural features[7] have also been shown to be stable to aqueous alkali. Structural support for the quinolizinium salts was

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(4) W. Sobtka, W. N. Beverung, G. G. Munoz, J. C. Sircar, and A. I. Meyers, *J. Org. Chem.*, **30**, 3667 (1965); N. D. Heindel, T. A. Brodof, and J. E. Kogelshatz, *J. Heterocyclic Chem.*, **3**, 222 (1966).

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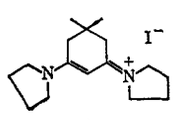
(6) Experiments designed to determine the utility of other metal ions for this reaction were performed. The results, using either silver perchlorate or cupric bromide gave tarry, polymeric, unidentifiable products along with starting materials.

(7) N. J. Leonard and J. A. Adamcik, *J. Am. Chem. Soc.*, **81**, 595 (1959). The authors described the isolation of A, which is analogous to compounds VI–VIII, from aqueous base by extraction with chloroform.



A

TABLE I

PHYSICAL DATA FOR AMINOBENZO[a]CYCLOALKANO[f]-QUINOLIZINIUM PERCHLORATES VI–VIII

Compd	VI	VII	VIII
Mp, °C	239 dec	252–254 dec	259–260 dec
λ_{max}^{EtOH}, mμ (ε)	346 (17,850)	353 (17,600)	353 (16,590)
λ^{Nujol}, μ	2.95, 3.07, 6.00, 6.13, 6.54	2.95, 3.08, 6.02, 6.29, 6.68	2.95, 3.03, 6.03, 6.22, 6.68
% yield	65	95	55
C, %			
Calcd	54.21	55.28	56.27
Found	53.93	55.07	56.42
H, %			
Calcd	5.81	6.10	6.38
Found	5.93	6.28	6.45
N, %			
Calcd	7.02	6.78	6.56
Found	7.03	6.89	6.58
Cl, %			
Calcd	8.89	8.59	8.30
Found	8.89	8.48	8.08

gathered by hydrolysis to the known enamino ketones (IX–XI).

Experimental Section

All melting points are corrected. Infrared and ultraviolet spectra were taken on Beckman IR-5 and DB instruments, respectively. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

1-(Cyanomethyl)-5,6-dimethoxy-1,2,3,4-tetrahydroisoquinoline (II). A. N-(2,3-Dimethoxyphenethyl)cyanacetamide.—A solution of 24.5 g of 2-(2,3-dimethoxyphenyl)ethylamine[8] and 90 ml of ethyl cyanacetate was heated at 115–120° for 20 hr under a slow stream of nitrogen. The excess cyanoacetic ester was removed *in vacuo* leaving a crystalline residue. Recrystallization from ether–chloroform gave 27 g (80%) of the amide: mp 94–95°; λ^{CHCl_3} 2.88, 2.96, 4.42, 5.93, 6.32, 6.60, 6.78, 6.94 μ; nmr ($CDCl_3$), τ 2.83–3.35, (multiplet, aromatic and amide, 4 H), 6.15 (singlet, methoxyls, 6 H), 6.35–6.75 (multiplet, CH_2NHCO-CH_2CN, 4 H), 7.0–7.30 (triplet, benzylic, 2 H).

Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.72; H, 6.65; N, 11.50.

B. 1-(Cyanomethyl)-5,6-dimethoxy-3,4-dihydroisoquinoline.—To a refluxing solution of 27 g of N-(2,3-dimethoxyphenethyl)-cyanoacetamide in 450 ml of dry toluene was added, in three portions, 90 g of phosphorus pentoxide. The reaction mixture was stirred and refluxed for 1.5 hr after which it was cooled to −10° and decomposed with 750 ml of ice water. The aqueous layer was separated and the organic layer was extracted several times with dilute hydrochloric acid. The acid solution was neutralized with 40% sodium hydroxide and the solvent was removed to yield 10 g (40%) of the dihydroisoquinoline: mp 200–202°; λ_{max}^{EtOH} 329, 272 mμ; λ^{CHCl_3} 2.90, 4.56, 6.20, 6.40, 6.85 μ. A neutral portion on evaporation gave 14 g of the starting cyanoacetamide mp 93–94°.

C. 1-(Cyanomethyl)-5,6-dimethoxy-1,2,3,4-tetrahydroisoquinoline.—A solution of 10 g of the above dihydroisoquinolinenitrile in 130 ml of acetic acid, containing 300 mg of platinum oxide was hydrogenated at 53 psi at room temperature for 20 hr. The catalyst was removed and the residue was dissolved in ice water, neutralized with potassium carbonate, and extracted with chloroform. The chloroform extract was washed with water and dried (sodium sulfate) and the solvent was removed to give a dark oil. The latter was dissolved in chloroform–ether (1:4) and filtered through alumina (30 g). Removal of solvent gave a solid which was recrystallized from dry ether as white flakes: yield, 6.8 g; nmr ($CDCl_3$), τ 3.18 (singlet, aromatic, 2 H), 5.50–5.82 (triplet, CHNH, 1 H), 6.18, 6.21 (singlets, methoxy, 3 H each), 6.77–7.30 (multiplet, methylenes, 6 H), 8.0 (broad singlet, NH, 1 H) exchangeable with D_2O.

Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.02; H, 6.87; N, 12.18.

(8) A. Lindenmann, *Helv. Chim. Acta*, **32**, 69 (1949).

7-Amino-3′,4′-dimethoxybenzo[a]cycloalkano[f]-1,5,6,9-tetrahydroquinolizinium Perchlorates VI–VIII.—A solution of 5 mmoles of the isoquinolinyl acetonitrile (II) in a tenfold excess of cycloalkanone and 20 ml of toluene containing a few crystals of *p*-toluenesulfonic acid was treated with 5.5 mmoles of anhydrous magnesium perchlorate and the mixture was refluxed under nitrogen for 40 hr. At the end of this period the crystalline magnesium perchlorate was transformed to an amorphous powder. The cold reaction mixture was shaken with 15 ml of a saturated solution of ammonium chloride and 5 ml of 40% sodium hydroxide solution at which time either a crystalline or a gummy solid separated. The solid was washed thoroughly with water and then with chloroform and dried. The crude product was recrystallized from anhydrous methanol.

Benzo[a]cycloalkano[f]quinolizinones IX–XI.—A mixture of 0.5 mmole of the 7-aminobenzo[a]cycloalkano[f]-1,5,6,9-tetrahydroquinolizinium perchlorates (VI–VIII) and 10 ml of 10% aqueous methanolic (1:3) sodium hydroxide solution was refluxed for 1.5–2.0 hr at which time a clear solution was obtained. Methanol was evaporated under reduced pressure and the residue was diluted with water, filtered, and washed thoroughly with water and dried. The product was sufficiently pure that, on admixture with authentic samples,[4] melting points were undepressed. The yields of IX–XI were 85–91%.

Registry No.—N-(2,3-Dimethoxyphenethyl)cyanacetamide, 7634-84-6; 1-(cyanomethyl)-5,6-dimethoxy-3,4-dihydroisoquinoline, 7634-85-7; II, 7634-86-8; VI, 7634-87-9; VII, 7634-88-0; VIII, 7634-89-1.

An Intramolecular Curtius Reaction of Some Hydroxy Amino Acids

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A well-known complication in the synthesis of serine peptides from carbobenzoxyserine azide is the rearrangement of the azide to an oxazolidinone (I) through the intermediate isocyanate.[1,2] This undesirable side reaction is usually avoided by maintaining adequate cooling during the formation and subsequent initial reaction of the azide with an amine function. It became of interest to us to determine if the carbobenzoxy group could be removed from this compound and the resulting unknown 4-amino-2-oxazolidinone isolated and identified.

Cyclization was readily performed by allowing an ethyl acetate solution of carbobenzoxyserine azide to stand at room temperature for a few hours. Catalytic hydrogenation of the resulting oxazolidinone in ethanol solution using palladium on carbon rapidly removed the carbobenzoxy group and on standing the solution developed a strong odor of ammonia. A crystalline solid was isolated which gave strong bands at 1030, 1736, and 3356 cm^{-1} in the infrared. The absence of a band at 1550 cm^{-1} supported the view that the oxazolidinone structure was still intact.[3,4] Analysis indicated a condensation product minus 1 mole of ammonia. The structure postulated for the product, 4,4′-iminodi-2-oxazolidinone (II), was supported by the

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