Department of Chemistry and Pharmaceutical Chemistry
School of Pharmacy, Medical College of Virginia

The Synthesis of 2-Aryl-3-oxa-1-azaspiro[4.4]non-1-enes (1) (2)

Paul W. Collins (3) and John Andrako

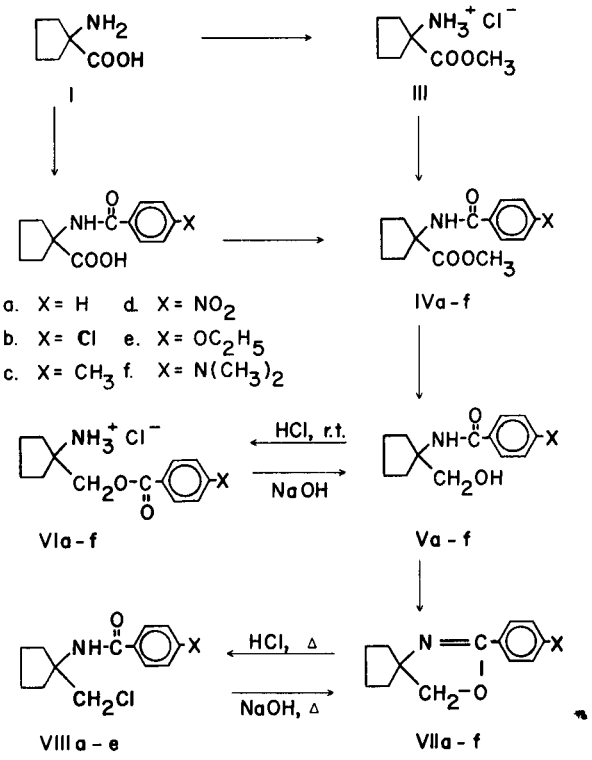
A series of 2-aryl-3-oxa-1-azaspiro[4.4]non-1-enes was prepared by cyclization of the corresponding β-acylamino alcohols (V) with thionyl chloride. Structure proofs for the β-acylamino alcohols and the spiro compounds are given. Infrared and p.m.r. data are reported.

Numerous and diverse physiological activities are found among 2-oxazoline compounds (4a-g). A variety of medicinal properties have been reported (5a-b) also for a number of heterocyclic spiro compounds. Having found no reports of 4-spiro-2-aryl-2-oxazolines in the literature, we were prompted to prepare the present series of 2-aryl-3-oxa-1-azaspiro[4.4]non-1-enes (1) on the basis of their potential pharmacological interest.

The synthesis of this series of compounds was accomplished by the indicated sequence of reactions. The amido esters (IVa-e) (Table I) were prepared by esterification of the corresponding amido acids (II) which were obtained by acylation of 1-aminocyclopentane-1-carboxylic acid (6) (I). Complete removal of the corresponding *p*-substituted benzoic acids (formed from the acyl chlorides) from the amido acids (II) proved to be difficult. As a result, the amido acids were not characterized (except for 1-benzamidocyclopentane-1-carboxylic acid) (6) but were converted directly to the amido esters (IVa-e) which were purified much more easily. IVa and IVe were prepared also by acylation of 1-amino-1-carbomethoxycyclopentane (6) (III). Dicyclohexylcarbodiimide was used to prepare IVf from *p*-dimethylaminobenzoic acid and III after attempts to prepare it by the mixed carbonic anhydride method had failed.

Lithium borohydride was employed to reduce the amido esters (IVa-f) to the corresponding amido alcohols (Va-f) (Table II). The success of the reductions was ascertained by examination of the infrared spectra which were essentially void of absorption in the ester carbonyl region but showed absorption corresponding to an alcoholic hydroxyl group. All the amido alcohols Va-f), on treatment with chloroform saturated with hydrogen chloride gas, rearranged by *N* to *O* acyl migration to the corresponding 1-amino-1-cyclopentylmethyl *p*-substituted benzoate hydrochlorides (VIa-f) (Table III). On treatment with dilute sodium hydroxide solution the hydrochlorides (VIa-f) rearranged to the amido alcohols (Va-f) by *O* to *N* acyl migration. This sequence of reactions provided further evidence for the structure of the amido alcohols of Table II.

The oxazoline spirans (VIIa-f) (Table IV) were obtained as their hydrochlorides by treatment of the amido alcohols (V) with thionyl chloride. The yields in Table IV are based on the amounts of the hydrochlorides obtained except for VIe and VIf whose hydrochlorides were too hygroscopic to isolate without great difficulty. The principal features of the infrared spectra of the oxazoline spirans are the presence of an absorption band between 6.06 and 6.12 μ corresponding to the imine (C=N) group (7) of the oxazoline ring and the virtual absence of absorption in the alcoholic OH and amide NH regions (2.75-3.25 μ) of the spectrum. In addition to these features, the infrared spectra of the oxazoline hydrochlorides display a broad absorption band between 3.7 and 4.35 μ corresponding to the "ammonium" band of the $C=\overset{+}{N}H$ group (7).



The p.m.r. spectrum (8) (deuteriochloroform) of VIIe is given in figure 1. Integrated areas under the aromatic, etheric and alkyl absorption peaks are in the ratio 4:4:11, in agreement with the assigned structure.

The oxazoline compounds (VIIa-e) were converted to the corresponding 1-(*p*-substituted benzamido)-1-chloromethylcyclopentanes (VIIIa-e) (Table V) by treatment with a saturated solution of hydrogen chloride in dioxane. The β-chloroamides (VIIIa, b, c, and e) were converted to the corresponding oxazoline compounds by treatment with alkali. Thus the oxazoline structure of the compounds of Table IV was confirmed.

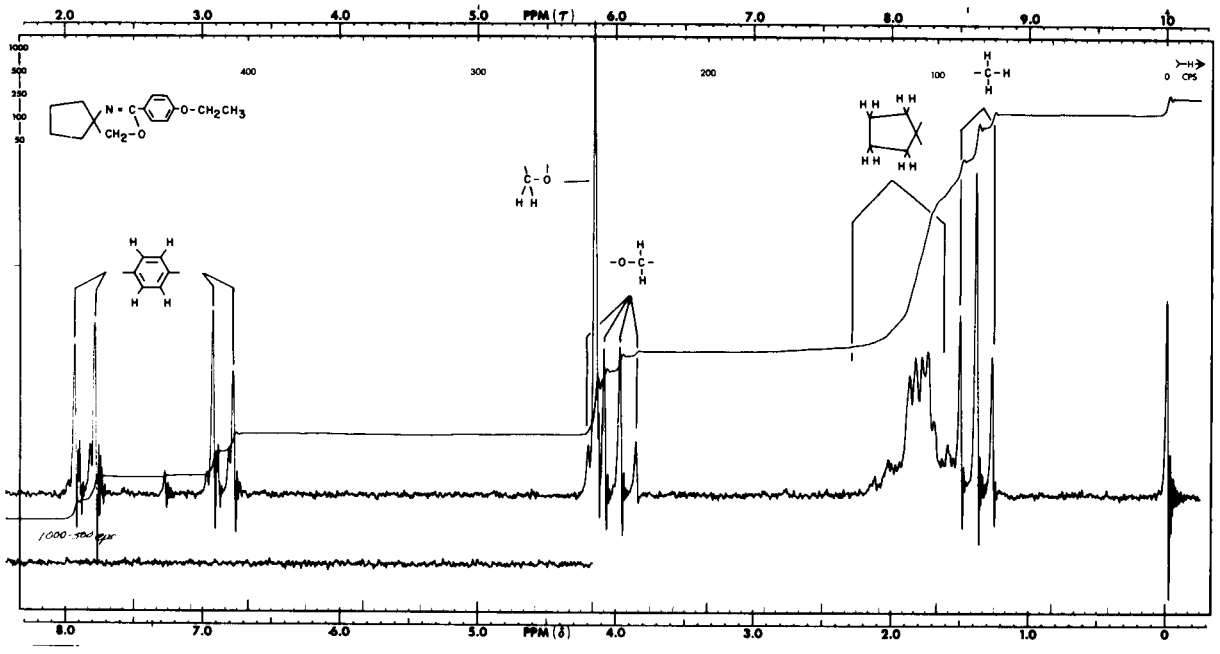


Fig. 1. P.m.r. spectrum of 2-*p*-ethoxyphenyl-3-oxa-1-azaspiro[4.4]non-1-ene (VIIe).

TABLE I

1-(*p*-Substituted Benazmido)-1-carbomethoxycyclopentanes

Compound	X	M.p. °C	Crystn. solvent	Method	Yield %	Formula	Carbon % Calcd.	Carbon % Found	Hydrogen % Calcd.	Hydrogen % Found	Nitrogen % Calcd.	Nitrogen % Found
IVa	H	121.5-123	Benzene-Ligroin	A, B	83(A) 56(B)	$C_{14}H_{17}NO_3$	68.01	68.11	6.88	7.18	5.66	5.39
IVb	Cl	143-145	Acetone-Water	A	82	$C_{14}H_{16}ClNO_3$	59.68	60.06	5.68	6.19	4.97	5.08
IVc	CH_3	117-119	Benzene-Ligroin	A	65	$C_{15}H_{19}NO_3$	68.97	68.85	7.27	7.29	5.36	5.32
IVd	NO_2	165.5-167	Benzene-Ligroin	A	62	$C_{14}H_{16}N_2O_5$	57.53	57.46	5.47	5.68	9.58	9.43
IVe	OC_2H_5	122-123	Benzene-Ligroin	A, C	56(A) 79(C)	$C_{16}H_{21}NO_4$	65.95	65.96	7.21	7.47	4.81	4.86
IVf	$N(CH_3)_2$	154.5-156	50% Ethanol	D	65	$C_{16}H_{22}N_2O_3$	66.21	66.10	7.59	7.73	9.65	9.60
IVf	HCl $N(CH_3)_2$	188.5-191.5	Ethanol-Ether			$C_{16}H_{23}ClN_2O_3$	58.81	58.83	7.04	7.73	8.57	8.56

TABLE II

1-(*p*-Substituted Benzamido)-1-hydroxymethylcyclopentanes

Compound	X	M.p.°C	Crystn. solvent	Yield %	Formula	Carbon % Calcd.	Carbon % Found	Hydrogen % Calcd.	Hydrogen % Found	Nitrogen % Calcd.	Nitrogen % Found
Va	H	119-121	Benzene-Ligroin	83	$C_{13}H_{17}NO_2$	71.23	71.18	7.76	7.96	6.39	6.42
Vb	Cl	162-164.5	Benzene-Ligroin	85	$C_{13}H_{16}ClNO_2$	61.53	61.57	6.31	6.47	5.52	5.48
Vc	CH_3	122.5-124.5	Benzene-Ligroin	74	$C_{14}H_{19}NO_2$	72.10	72.13	8.15	8.30	6.01	6.15
Vd	NO_2	193.5-195	Acetone-Water	71	$C_{13}H_{16}N_2O_4$	59.09	59.09	6.10	6.10	10.61	10.74
Ve	OC_2H_5	94.5-95.5	60% Ethanol	76	$C_{15}H_{21}NO_3$	68.44	68.27	7.98	7.97	5.32	5.45
Vf (a)	$N(CH_3)_2$	133-134.5	Benzene-Ligroin	82	$C_{15}H_{22}N_2O_2$	68.70	68.80	8.39	8.72	10.67	10.81

(a) The hydrochloride melts at 160-162°; *Anal.* Calcd. for $C_{15}H_{23}ClN_2O_2$: N, 9.38. Found: N, 9.21.

TABLE III

1-Amino-1-cyclopentylmethyl *p*-Substituted Benzoate Hydrochlorides

Compound	X	M.p.°C	Crystn. solvent	Yield %	Formula	Carbon % Calcd.	Carbon % Found	Hydrogen % Calcd.	Hydrogen % Found	Nitrogen % Calcd.	Nitrogen % Found
VIa	H	230.5-231.5 dec.	Acetone-Ethanol	70	$C_{13}H_{18}ClNO_2$	61.06	60.93	7.04	7.30	5.48	5.53
VIb	Cl	279.5-281 dec.	Ethanol-Ether	73	$C_{13}H_{17}Cl_2NO_2$	53.79	53.99	5.86	6.18	4.82	4.81
VIc	CH_3	253.5-254.5 dec.	Ethanol-Ether	80	$C_{14}H_{20}ClNO_2$	62.34	62.52	7.42	7.63	5.19	5.01
VId	NO_2	245.5-246.5 dec.	Ethanol-Ether	65	$C_{13}H_{17}ClN_2O_4$	51.91	51.67	5.65	5.95	9.31	9.36
VIe	OC_2H_5	222-223 dec.	Ethanol-Ether	71	$C_{15}H_{22}ClNO_3$	60.10	60.12	7.34	7.75	4.67	4.48
VIf	$N(CH_3)_2$	240-241.5 dec.	Ethanol-Ether	63	$C_{15}H_{24}Cl_2N_2O_2$					8.36	8.21

TABLE IV

2-Aryl-3-oxa-1-azaspiro[4.4]non-1-enes (1)

Compound	X	M.p.°C	Crystn. solvent	Yield %	Formula	Carbon % Calcd.	Carbon % Found	Hydrogen % Calcd.	Hydrogen % Found	Nitrogen % Calcd.	Nitrogen % Found
VIIa	H	liquid			$C_{19}H_{18}N_4O_8$ (a)	53.02	52.97	4.16	4.46	13.02	12.67
VIIa HCl	H	135-136	CH_2Cl_2-Ether	94	$C_{13}H_{16}ClNO$	65.68	65.68	6.74	6.77	5.91	5.87
VIIb	Cl	61-62	50% Ethanol		$C_{13}H_{14}ClNO$	66.24	66.46 (b)	5.95	6.13 (b)	5.95	5.86
VIIb HCl	Cl	128.5-129.5	CH_2Cl_2-Ether	81	$C_{13}H_{15}Cl_2NO$	57.35	57.34 (b)	5.51	5.65 (b)	5.15	5.21 (b)
VIIc	CH_3	29.5-31	Acetone-Water		$C_{14}H_{17}NO$					6.51	6.49
VIIc HCl	CH_3	121.5-122.5	CH_2Cl_2-Ether	67	$C_{14}H_{18}ClNO$	68.80	68.58 (c)	7.16	7.13 (c)	5.57	5.66 (c)
VIId	NO_2	75-77	Acetone-Water		$C_{13}H_{14}N_2O_3$	63.41	63.33 (c)	5.69	5.97 (c)	11.38	11.20 (c)
VIId HCl	NO_2	120-121.5	CH_2Cl_2-Ether	86	$C_{13}H_{15}ClN_2O_3$	55.22	55.57 (b)	5.31	5.38 (b)	9.91	10.04 (b)
VIIe	OC_2H_5	80-81	50% Ethanol	61	$C_{15}H_{19}NO_2$	73.47	73.28	7.75	7.98	5.71	5.74
VIIf	$N(CH_3)_2$	108-110	Acetone-Water	82	$C_{15}H_{20}N_2O$	73.77	73.93 (b)	8.88	8.42 (b)	11.47	11.67 (b)

(a) Analyzed as the picrate, m.p. 175-177°. (b) Analysis done by Micro-Tech Labs., Skokie, Illinois. (c) Analysis done by Triangle Labs., Chapel Hill, N. C.

TABLE V

1-(*p*-Substituted Benzamido)-1-chloromethylcyclopentanes

Compound	X	M.p. °C	Crystn. solvent	Formula	Nitrogen % Calcd.	Found
VIIIa (a)	H	126.5-127.5	Acetone-Water	$C_{13}H_{16}ClNO$	5.91	5.71
VIIIb	Cl	107-108	Methanol-Water	$C_{13}H_{15}Cl_2NO$	5.15	5.07
VIIIc	CH_3	100-101	Acetone-Water	$C_{14}H_{18}ClNO$	5.57	5.50
VIIId	NO_2	147-149	Acetone-Water	$C_{13}H_{15}ClN_2O_3$	9.91	9.60
VIIIe	OC_2H_5	105-106	Acetone-Water	$C_{15}H_{20}ClNO_2$	4.97	4.91

(a) *Anal.* Calcd. for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.74. Found: C, 65.48; H, 6.89.

EXPERIMENTAL (9)

1-Aminocyclopentane-1-carboxylic acid (I).

This compound described by Conners and Ross (6) was prepared by acid hydrolysis of the corresponding hydantoin according to the general procedure described by Goodson *et al.*, (10).

1-Amino-1-carbomethoxycyclopentane (III).

This compound was prepared according to the procedure described by Conners and Ross (6).

1-Benzamidocyclopentane-1-carboxylic acid (II).

To a 1 l., three-necked, round-bottomed flask equipped with a mechanical stirrer were added 43 g. (0.33 mole) of 1-aminocyclopentane-1-carboxylic acid (6) and 165 ml. of 2 *N* sodium hydroxide. The flask was placed in an ice bath, and the solution was stirred vigorously while 40 ml. of benzoyl chloride and 165 ml. of 2 *N* sodium hydroxide were added from separate dropping funnels over a 2 hour period. The reaction mixture was stirred for two additional hours after all the reactants had been added. The solution was made acidic with 5 *N* hydrochloric acid and the resulting precipitate was collected on a Buchner funnel and air dried. Recrystallization from 75% ethanol afforded 48 g. (62%) of 1-benzamidocyclopentane-1-carboxylic acid, m.p. 214-215° (lit. 214-215° (6)).

Other acids were prepared in a similar manner.

1-Benzamido-1-carbomethoxycyclopentane (IVa) (Table I). Method A.

A mixture of 16.0 g. (0.07 mole) of 1-benzamidocyclopentane-1-carboxylic acid in 20 ml. of methanol, 50 ml. of 2,2-dimethoxypropane and 2 ml. of concentrated hydrochloric acid was stirred for 30 hours at room temperature. The reddish-brown solution was then evaporated to dryness. The residue was washed with dilute aqueous sodium hydroxide to remove starting material and with ligroin to remove the color. Recrystallization from benzene-ligroin afforded 14 g. (83%) of IVa, m.p. 121.5-123°; infrared absorptions were present at 2.96 μ (NH), 5.77 μ (ester C=O), and 6.14 μ (amide C=O).

Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 68.01; H, 6.88; N, 5.66. Found: C, 68.11; H, 7.18; N, 5.39.

Compounds IVb-e were prepared in a similar manner.

Method B.

Benzoyl chloride (7.0 g.) was added in portions to a stirred solution of 9.0 g. (0.05 mole) of 1-amino-1-carbomethoxycyclopentane hydrochloride (3) (III hydrochloride) in 40 ml. of pyridine. The solution was heated to 100° for 20 minutes, cooled, and diluted with 50 ml. of water. The diluted solution was extracted several times with ether. The combined extracts were washed successively with dilute hydrochloric acid and water, dried (sodium sulfate) and evaporated to dryness. Recrystallization of the residue from benzene-ligroin gave 7.0 g. (56%) of IVa, m.p. 121.5-123°. The infrared spectrum of this compound is identical with that of the product (IVa) from Method A. There was no depression in the melting point of a mixture of the two products.

1-(*p*-Ethoxybenzamido)-1-carbomethoxycyclopentane (IVe). Method C.

A mixture of 15.0 g. (0.083 mole) of III hydrochloride in 100 ml. of water and 16.0 g. of *p*-ethoxybenzoyl chloride in 175 ml. of chloroform was placed in a 1 l. volumetric flask and subjected to mechanical shaking for 24 hours. During this period 16.0 g. (0.19 mole) of sodium bicarbonate was added to the mixture in portions. The chloroform layer was removed at the end of the reaction period, and the water layer was extracted several times with chloroform. The original chloroform layer and the extracts were combined, washed successively with dilute hydrochloric acid and water, dried (sodium sulfate) and evaporated to dryness. The yellow residue was washed with ligroin and recrystallized from benzene-ligroin to give 19.0 g. (79%) of IVe, m.p. 122-123°. The infrared spectrum of this compound is identical with that of authentic IVe obtained by Method A.

1-(*p*-Dimethylaminobenzamido)-1-carbomethoxycyclopentane (IVf). Method D.

To a vigorously stirred suspension of 9.0 g. (0.05 mole) of III hydrochloride in 500 ml. of dichloromethane were added succesively 5.1 ml. (0.05 mole) of triethylamine, 8.25 g. (0.05 mole) of *p*-dimethylaminobenzoic acid and 10.5 g. (0.055 mole) of dicyclohexylcarbodiimide. The reaction mixture was stirred for 48 hours at room temperature. It was then filtered to remove dicyclohexylurea, and the filtrate was evaporated to dryness. The residue was washed several times with 1 *N* hydrochloric acid and the acid solutions were combined, decolorized with charcoal, and filtered. The filtrate was made distinctly alkaline with 2 *N* sodium hydroxide and the resulting precipitate was collected on a Buchner funnel and washed well with water. Recrystallization from 50% ethanol afforded 9.5 g. (65%) of IVf, m.p. 154.5-156°. The infrared spectrum displays an ester and an amide carbonyl peak.

Anal. Calcd. for $C_{16}H_{22}N_2O_3$: C, 66.21; H, 7.59; N, 9.65. Found: C, 66.10; H, 7.73; N, 9.60.

1-Benzamido-1-hydroxymethylcyclopentane (Va) (Table II).

A suspension of 2.2 g. (0.04 mole) of potassium borohydride and 2.4 g. (0.055 mole) of anhydrous lithium chloride in 100 ml. of tetrahydrofuran (THF) was placed in a 300 ml. round-bottomed flask which was equipped with a magnetic stirrer and a reflux condenser fitted with a calcium chloride drying tube. The suspension was stirred for 8 hours at room temperature. A solution of 10 g. (0.04 mole) of IVa in 25 ml. of THF was added, and the mixture was refluxed for 10 hours. After the mixture had cooled to room temperature, 25 ml. of water was added in portions and stirring was continued for several hours until evolution of hydrogen was no longer evident. The THF layer was separated, and the aqueous layer was extracted several times with THF. The original THF layer and the extracts were combined, dried (sodium sulfate) and evaporated to dryness. After recrystallization from benzene-ligroin, there was obtained 7.3 g. (83%) of Va, m.p. 119-121°; infrared absorption bands were present at 2.96 and 3.04 μ (NH and OH), and 6.14 μ (amide C=O). No absorption bands occurred in the ester C=O region of the spectrum.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.23; H, 7.76; N, 6.39. Found: C, 71.18; H, 7.96; N, 6.42.

Compounds Vb-f (Table II) were prepared in a similar manner.

1-Amino-1-cyclopentylmethyl Benzoate Hydrochloride (VIa) (Table III) by *N* - *O* Acyl Migration.

A solution of Va (1.0 g.) in 50 ml. of chloroform was saturated with gaseous hydrogen chloride and allowed to stand at room temperature in a stoppered flask for 24 hours. The solution was then evaporated to dryness. The residue was washed with ether to remove starting material, and recrystallized from acetone-ethanol to yield 0.88 g. (70%) of VIa, m.p. 230.5-231.5° dec.; infrared absorption bands were present at 3.1 to 4.0 μ (ammonium band), and 5.80 μ (ester C=O). No absorption was present in the amide C=O region.

Anal. Calcd. for $C_{13}H_{18}ClNO_2$: C, 61.06; H, 7.04; N, 5.48. Found: C, 60.93; H, 7.30; N, 5.53.

Compounds VIb-f (Table III) were prepared essentially in the same manner.

1-Benzamido-1-hydroxymethylcyclopentane (Va) by *O* - *N* Acyl Migration.

A solution of VIa (0.5 g.) in 10 ml. of water was made distinctly alkaline with 1 *N* sodium hydroxide. The cloudy solution was refrigerated for 1 hour and then filtered. The solid which was collected was recrystallized from benzene-ligroin to give a material melting at 119-121°. The infrared spectrum of this material was identical with that of authentic Va (Table II). There was no depression in the melting point of a mixture of the two compounds.

Compounds VIb-f were converted to their respective amides, Vb-f, in a similar manner.

2-Phenyl-3-oxa-1-azaspiro[4.4]non-1-ene; (2-Phenyl-2-oxazoline-4-spirocyclopentane) (VIIa) (Table IV).

Five grams (0.023 mole) of Va was added to a 125 ml. conical flask containing 20 ml. of benzene. Thionyl chloride (60 ml.) was added in portions to the flask which during the addition was maintained at a temperature below 10° and shaken intermittently. The flask was stoppered and allowed to stand at room temperature for 24 hours. The solution was then poured into 300 ml. of cold purified ether which was stirred vigorously during the addition. The white solid which precipitated was collected on a sintered glass funnel, washed well with purified ether, and recrystallized from dichloromethane-ether to give 5.1 g. (94%) of VIIa hydrochloride, m.p. 135-136°; infrared absorption bands were present at 3.7 to 4.4 μ ("ammonium" band of $C=\overset{+}{N}H$ group) and 6.15 μ (C=N).

Anal. Calcd. for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.74; N, 5.91. Found: C, 65.68; H, 6.77; N, 5.87.

Compounds listed in Table IV were prepared similarly.

1-Benzamido-1-chloromethylcyclopentane (VIIIa) (Table V).

A solution of 2.3 g. of VIIa hydrochloride in 40 ml. of dioxane was saturated with gaseous hydrogen chloride and refluxed for 45 minutes. The solution was cooled and evaporated to dryness. The residue was washed with water and recrystallized from acetone-water to afford VIIIa, m.p. 126.5-127.5°; infrared absorption bands were present at 2.94 μ (NH) and 6.13 μ (amide C=O).

Anal. Calcd. for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.74; N, 5.91. Found: C, 65.48; H, 6.89; N, 5.71.

Compounds VIIIb-e were prepared in a similar manner.

2-Phenyl-3-oxa-1-azaspiro[4.4]non-1-ene (VIIa) from 1-Benzamido-1-chloromethylcyclopentane (VIIIa).

A suspension of 300 mg. of VIIIa in 6 ml. of 70% ethanol containing 80 mg. of sodium hydroxide was heated on a steam bath for 3 minutes. The hot solution was placed in an ice bath and diluted with 5 ml. of water. The solution was acidified with dilute hydrochloric acid and extracted with ether to remove starting material. The solution was made alkaline with 1 *N* sodium hydroxide and extracted several times with ether. The combined extracts were dried (sodium sulfate) for 48 hours and then treated with gaseous hydrogen chloride to precipitate a material which, after recrystallization from dichloromethane-ether, melted at 135-136°. The infrared spectrum of this compound was identical with that of authentic VIIIa. There was no depression in the melting point of a mixture of the two compounds.

VIIIb, c and e were converted to the corresponding oxazolines in a similar manner.

REFERENCES

(1) Although not preferred by Chemical Abstracts, another acceptable name for these compounds is 2-aryl-2-oxazoline-4-spirocyclopentanes.

(2) Taken in part from the Ph.D. Thesis, P. W. Collins, Medical College of Virginia (1966).

(3) Trainee, National Institutes of Health Training Grant, 5 T1-GM-484.

(4a) J. W. Cornforth, in "Heterocyclic Compounds", R. C. Elderfield, Ed., Vol. 5, John Wiley and Sons, New York, N. Y., 1957, p. 377; (b) B. Belleau and D. J. Triggle, *Can. J. Chem.*, **40**, 1201 (1962); (c) P. L. deBenneville and L. S. Luskin, German Patent, 1,067,437 (1959); *Chem. Abstr.*, **55**, 19960a (1961); (d) L. Anigstein and D. M. Whitney, *Texas Rep. Biol. Med.*, **10**, 768 (1952); (e) G. I. Poos, J. R. Carson, J. D. Rosenau, A. P. Roszkowski, N. M. Kelly and J. McGowin, *J. Med. Chem.*, **6**, 266 (1963); (f) R. B. Moffett, *J. Med. Chem.*, **7**, 319 (1964); (g) V. Rosnati and D. Misiti, *Rend. Ist. Super. Sanita*, **23**, 620 (1960).

(5a) L. M. Rice, C. F. Geschickter and C. H. Grogan, *J. Med. Chem.*, **6**, 388 (1963); (b) C. H. Grogan, C. F. Geschickter, M. E. Freed and L. M. Rice, *J. Med. Chem.*, **8**, 62 (1965).

(6) T. A. Conners and W. C. J. Ross, *J. Chem. Soc.*, 2119 (1960).

(7) K. Nakanishi, "Infrared Absorption Spectroscopy- Practical", Holden-Day Inc., San Francisco, Calif., 1962, p. 38.

(8) Obtained with a Varian Assoc. Model A60 NMR Spectrometer, through the courtesy of the A. H. Robins Co., Richmond, Va.

(9) All melting points were obtained with a Thomas-Hoover capillary melting point apparatus and are uncorrected. All analyses were performed at the Medical College of Virginia, Richmond, Virginia unless otherwise indicated. All infrared spectra were obtained with a Perkin-Elmer Model 137 Infracord spectrophotometer. All samples were examined as potassium bromide discs unless otherwise stated.

(10) L. H. Goodson, I. L. Honigberg, J. J. Lehman and W. H. Burton, *J. Org. Chem.*, **25**, 1920 (1960).

Received June 1, 1966 Richmond, Virginia 23219