The anhydrous compound was obtained by drying *in vacuo* at 140° for two days, m.p. 170°, $[\alpha]^{20}D$ −68.6° (*c* 1.0, dimethylformamide).

Anal. Calcd. for $C_{26}H_{33}O_5N_3S_2$: C, 58.75; H, 6.26; N, 7.91; S, 12.06; amide N, 2.63. Found: C, 58.46; H, 6.47; N, 7.90; S, 12.32; amide N, 2.08.[24]

(24) A portion of the ammonia was lost by foaming; insufficient material was available for a second determination.

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[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CIBA PHARMACEUTICAL PRODUCTS, INC.]

Antihypertensively Active Amidoximes

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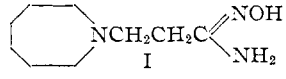
Hexahydro-1-azepinepropionamidoxime and structurally related compounds were prepared and were found to have prolonged antihypertensive properties. Maximum activity was noted with the hexahydroazepine ring compound; this activity diminished as the ring size was altered. Variation of the propionamidoxime side chain likewise resulted in a lessening of activity.

The chemotherapy of the amidoximes has been the subject of several recent papers. Lamb and White[3] have studied the antitrypanosomal activity of alkylene diamidoximes and diamidoximes derived from biphenyl, diphenylmethane and related compounds.

The literature[4] also reports that *p*-sulfamylbenzamidioxime exhibits pronounced antirickettsial activity on experimental typhus infections in mice; acetamidoxime thionocarbamates of morpholine and piperidine have been studied for their antibacterial and antifungal properties.[5]

Buu-Hoï,[6] *et al.*, found that halogenated salicylamidoximes display considerable tuberculostatic properties *in vitro;* the pyridineamidoximes were found to be inactive.[7]

The literature does not disclose a similar interest in the pharmacology of the amidoximes. In the case of hexahydro-1-azepinepropionamidoxime (I), however, a unique antihypertensive activity has been noted.[8]



I

A study of its effects on the cardiovascular system of the dog revealed that a single intravenous dose of 30 mg./kg. lowered the arterial pressure of neurogenic and renal hypertensive dogs. However, in normotensive animals 30 mg./kg. of the compound given intravenously eliminated the severe hypertension elicited by high doses of amphetamine and ephedrine and also markedly antagonized carotid occlusion reflex pressor responses. These antihypertensive effects were slow in onset and lasted for approximately two to six weeks following single injection. The compound was found to be orally active and had a cumulative action when given in small daily doses.

The relationship of ring size to antihypertensive activity in this class of compounds was found to be quite critical. For example, the 1-pyrrolidine and 1-piperidinepropionamidoximes were almost devoid of antihypertensive activity, whereas the corresponding hexahydroazepine derivative was most active. With further ring enlargement activity gradually diminished and was totally absent in the eleven-membered ring compound, 1-azacycloundecanepropionamidoxime. Modification of the azepine ring by substitution or formation of tetrahydro-3,1H-benzazepine failed to give compounds with increased activity. Frequently these alterations caused reduction of activity. Replacement of the hexahydroazepinyl moiety by piperazinyl, di-2-pyridylamino, carbazolyl and other ring systems did not disclose any interesting pharmacological properties. Dialkylaminopropionamidoximes as well as other aliphatic amidoximes were prepared, but in all cases activity was absent. Consideration also was given to the amidoxime derivatives; in the case of the O-acyl compounds there was a noticeable retention of activity. Loss of activity occurred too when the amidoxime function in the hexahydroazepine side chain was replaced by a variety of other functional groups.

The most active member of the series was prepared by cyanoethylation of hexahydroazepine to give hexahydro-1-azepinepropionitrile.[9] Treatment of the latter compound with hydroxylamine in ethanol yielded the desired amidoxime which could be converted to an appropriate salt. The feasibility of preparing this compound from the hexahydro-2-oxo-1-azepinepropionamidoxime by lithium aluminum hydride reduction was investigated. It was found that in ether the reduction occurred without alteration of the amidoxime func-

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TABLE I

PROPIONITRILES, RCH_2CH_2CN

R	Yield, %	B.p., °C.	Mm.	$n^{30}D$	Molecular formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
4-Methyl-1-piperazinyl	72	91–108	0.15	1.4708	$C_8H_{15}N_3$	62.80	62.47	9.88	9.76	27.47	28.25
Di-2-pyridylamino	33	93–97[a]		....	$C_{13}H_{12}N_4$	69.70	69.56	5.40	5.37	25.01	24.84
Hexahydro-1-azepinyl	88	121–123	14	1.4710	$C_9H_{16}N_2$	71.11	70.82	10.61	10.52	18.43	18.53
Hexahydro-5-methyl-2-oxo-1-azepinyl	85	136–139	1	1.4786	$C_{10}H_{16}N_2O$					15.56	15.74
Hexahydro-4-methyl-1-azepinyl	72	129–130	15	1.4692	$C_{10}H_{18}N_2$	72.35	72.58	10.93	10.63	16.88	17.16
Octahydro-1-azocinyl	88	92–97	0.5	1.4778	$C_{10}H_{18}N_2$	72.35	72.51	10.93	10.99	16.88	16.63
Octahydro-1-azoninyl	82	83–85	1	1.4815	$C_{11}H_{20}N_2$	73.39	73.53	11.20	11.23	15.56	15.34
1-Azacycloundecyl	60	125–130	0.25	1.4784	$C_{13}H_{24}N_2$	75.06	75.24	11.63	11.62	13.47	13.29
2,3,4,5-Tetrahydro-3,1H-benzazepin-3-yl	74	61–64[b]		....	$C_{13}H_{16}N_2$	78.07	78.63	8.06	8.02	14.01	13.58

[a,b] Melting points; crystallized from [a] ethanol, and [b] aqueous ethanol.

tion and gave the desired hexahydro-1-azepinepropionamidoxime in good yield. Treatment of hexahydroazepine with 3-chloro-2-hydroxypropionitrile[10] failed to give a compound with the hydroxypropionitrile side chain. The corresponding acetaldehyde was obtained instead, even under very mild conditions. Although hexahydroazepine may be prepared by reduction of ϵ-caprolactam with lithium aluminum hydride,[11] sodium borohydride does not ordinarily reduce lactams. It was found, however, that treatment with sodium borohydride–aluminum chloride in diethylene glycol dimethyl ether (diglyme)[12] did effect reduction to the desired hexahydroazepine, but in low yields. The preparation of 4-(hexahydroazepine)-2-butanone by a Mannich reaction was successful, but when the conditions were altered, 2-acetyl-trimethylene-1,3-bis-(hexahydro-1-azepine) was obtained. It was found that the O-benzoyl derivative of hexahydro-1-azepinepropionamidoxime could be prepared, but that some other acyl derivatives were too hygroscopic for purification and reverted to the monohydrochloride of the starting amidoxime. Hexahydro-5-methyl-2-oxo-azepine was prepared by a Beckmann rearrangement, using benzenesulfonyl chloride for ring expansion.[13] In the other instances the Schmidt reaction, as recently detailed,[11b] was used. All reductions to the desired saturated large ring compounds were accomplished with lithium aluminum hydride.

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Experimental[14]

Table I lists those propionitriles not previously reported in the literature. 1-Pyrrolidinepropionitrile,[15] 1-piperidinepropionitrile,[16,17] 2-methyl-1-piperidinepropionitrile,[15] 2,6-dimethyl-1-piperidinepropionitrile,[15] 3-(di-*n*-propylamino)-propionitrile[16,18] and hexahydro-2-oxo-1-azepinepropionitrile[19] were prepared by methods which have been described. Tetrahydro-3,1H-benzazepine[20] was prepared from *o*-benzenediacetonitrile.

Details for the preparation of hexahydro-1-azepinepropionamidoxime are given to illustrate the general method used in preparing the amidoximes listed in Table II.

The cycloalkanones, required for the preparation of the various large-membered ring compounds, were obtained from the Aldrich Chemical Co.

Hexahydro-1-azepinepropionitrile.—To 212 g. (4 moles) of acrylonitrile was added slowly with stirring 50 g. (0.5 mole) of hexahydroazepine; 1 ml. of Triton B was then added cautiously and after the initial reaction subsided the mixture was refluxed for 2 hours. Stirring was continued overnight at room temperature, the excess acrylonitrile was removed *in vacuo* and the residual liquid fractionated to give 67.5 g. (88%) of a colorless oil, b.p. 121–123° (14 mm.), $n^{30}D$ 1.4710.

Anal. Calcd. for $C_9H_{16}N_2$: C, 71.11; H, 10.61; N, 18.43. Found: C, 70.82; H, 10.52; N, 18.53.

Hexahydro-1-azepinepropionamidoxime Dihydrochloride.—To 13.9 g. (0.2 mole) of hydroxylamine hydrochloride in 300 ml. of anhydrous ethanol was added 30.4 g. (0.2 mole) of the above nitrile. To this stirring mixture was added sodium ethoxide solution (from 4.6 g. of sodium and 150 ml. of anhydrous ethanol). After refluxing for 3 hours and standing at room temperature overnight, the solution was filtered and the filtrate gassed with hydrogen chloride. The precipitate was recrystallized from ethanol–ether to yield 36 g. (70%) of product, m.p. 183–185° dec.

Anal. Calcd. for $C_9H_{21}Cl_2N_3O$: C, 41.90; H, 8.20; N, 16.29; Cl, 27.49. Found: C, 42.14; H, 8.17; N, 15.99; Cl, 27.61.

The monohydrochloride salt melted at 164–166° dec. when recrystallized from ethanol.

Anal. Calcd. for $C_9H_{20}ClN_3O$: C, 48.74; H, 9.09; N, 18.95; Cl, 15.99. Found: C, 48.92; H, 9.05; N, 18.90; Cl, 16.49.

Preparation from hexahydro-2-oxo-1-azepinepropionamidoxime by reduction with lithium aluminum hydride was accomplished in the following manner.

By means of a continuous-return type of Soxhlet extractor, the hexahydro-2-oxo-1-azepinepropionamidoxime (7 g., 0.035 mole) was introduced into a slurry of 2.01 g. (0.53 mole) of lithium aluminum hydride in 1500 ml. of ether. The extraction process was maintained for 72 hours by refluxing the hydrogenation mixture while stirring. After cooling, 10 ml. of water-saturated ether was added dropwise and this was followed by an additional 20 ml. of water. The mixture was acidified with 5 *N* aqueous sulfuric acid and extracted three times with 200 ml. of ether. The aqueous layer was separated, made basic with 40% aqueous

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TABLE II

PROPIONAMIDOXIMES $RCH_2CH_2C(=NOH)NH_2$

R	Salt[b]	Yield, %	M.p., °C. (dec.)	Molecular formula	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
Pyrrolidyl	HCl	77	169–172	$C_7H_{16}ClN_3O$	21.66	21.10	18.28	17.92
Piperidyl	2HCl	75	182–187	$C_8H_{19}Cl_2N_3O$	17.21	16.92	29.04	29.00
2-Methyl-1-piperidyl	2HCl	55	164–167	$C_9H_{21}Cl_2N_3O$	16.29	16.23	27.49	27.65
2,6-Dimethylpiperidyl	2HCl	65	184–187	$C_{10}H_{21}Cl_2N_3O$	15.55	15.75	26.24	26.36
4-Methylpiperazinyl	3HCl	70	187–190	$C_8H_{21}Cl_3N_4O$	18.74	18.52	36.06	36.28
Di-2-pyridylamino	2HCl	46	203–206	$C_{13}H_{17}Cl_2N_5O$	21.22	21.17	21.49	22.03
Carbazolyl	HCl	72	198–200	$C_{15}H_{16}ClN_3O$	14.50	14.31	12.26	12.95
Hexahydro-2-oxo-1-azepinyl	HCl	50	190–192	$C_9H_{18}ClN_3O_2$	17.85	17.81	15.06	15.19
Hexahydro-1-azepinyl[a]	2HCl	70	183–185	$C_6H_{21}Cl_2N_3O$	16.29	15.99	27.49	27.61
Hexahydro-5-methyl-2-oxo-1-azepinyl	Base[c]	41	157–159	$C_{10}H_{19}N_3O_2$	19.73	19.90		
Hexahydro-4-methyl-1-azepinyl[a]	2HCl	50	165–170	$C_{10}H_{23}Cl_2N_3O$	15.45	15.47	26.07	26.52
Octahydro-1-azocinyl[a]	2HCl	65	180–185	$C_{10}H_{23}Cl_2N_3O$	15.45	15.38	26.07	25.86
Octahydro-1-azoninyl[a]	2HCl	64	173–176	$C_{11}H_{25}Cl_2N_3O$	14.69	14.40	24.80	24.95
1-Azacycloundecyl[a]	2HCl	43	158–160	$C_{13}H_{29}Cl_2N_3O$	13.38	13.53	22.58	22.33
2,3,4,5-Tetrahydro-3,1H-benzazepin-3-yl[a]	2HCl	49	231–235	$C_{13}H_{21}Cl_2N_3O$	13.72	13.84	23.19	23.01
3-Dimethylamino	2HCl	60	151–165	$C_5H_{15}Cl_2N_3O$	20.59	19.92	34.74	34.41
3-Di-*n*-propylamino	HCl	55	<25	$C_9H_{22}ClN_3O$	18.80	18.84	15.84	15.49
3-Amino	HCl	74	152–153	$C_3H_{10}ClN_3O$	30.02	29.54	25.33	24.81
3-Hydroxy	Base[d]	69	90–92	$C_3H_8N_2O_2$	26.94	26.65		
3-Methoxy	HCl	65	132–134	$C_4H_{11}ClN_2O_2$	18.12	17.85	22.93	22.84

[a] Infrared absorption spectra of these amidoxime hydrochlorides were determined in Nujol mull. The saturated heterocyclic compounds show two strong bands at approximately 1705 ks. (C=N) and 1630 ks. (N^+); when extensive hydrogen bonding occurs, as with 3-hydroxypropionamidoxime, a bathochromic shift of approximately 30 ks. occurs. [b] All recrystallizations were from ethanol–ether. [c] *Anal.* Calcd.: C, 56.38; H, 8.99. Found: C, 56.23; H, 9.00. [d] *Anal.* Calcd.: C, 34.64; H, 7.75. Found: C, 34.84; H, 7.88.

sodium hydroxide and extracted with chloroform. Concentration *in vacuo* and treatment of the yellow oil (4.7 g., 72%) with ethanolic hydrogen chloride gave a product which could be recrystallized from ethanol, m.p. 183–185° dec. This compound gave no depression of the melting point when mixed with the sample obtained above; the infrared spectra were likewise identical with bands at 1706 and 1633 ks.

Anal. Found: C, 42.01; H, 8.43; N, 16.22; Cl, 27.28.

The O-benzoyl derivative was prepared by adding, in the cold and with stirring, 2.29 g. (0.016 mole) of benzoyl chloride in 10 ml. of ether to 3 g. (0.016 mole) of the free base of hexahydro-1-azepinepropionamidoxime dissolved in 200 ml. of ether. After standing overnight, the solution was filtered and the crude product was recrystallized from ethanol–ether to give 3.8 g. (73%) of white crystalline material, m.p. 153–155°.

Anal. Calcd. for $C_{16}H_{24}ClN_3O_2$: C, 59.13; H, 7.44; N, 12.93. Found: C, 58.84; H, 7.34; N, 12.99.

The O-methyl derivative was prepared by adding the free base of hexahydro-1-azepinepropionamidoxime (18.5 g., 0.1 mole) to a cooled solution of freshly prepared sodium ethoxide (from 2.3 g. of sodium and 250 ml. of anhydrous ethanol). To this mixture was added 6.8 ml. (0.11 mole) of methyl iodide and after refluxing for 15 minutes, stirring was continued overnight. The ethanol was removed *in vacuo*, ice-water was added to dissolve inorganic salt and the oil was extracted with chloroform. After concentration, the residual oil was fractionated to give 6.5 g. (33%) of a pale yellow oil, b.p. 75–80° (0.5 mm.), $n^{27}D$ 1.4774.

Anal. Calcd. for $C_{10}H_{21}N_3O$: C, 60.35; H, 10.64; N, 21.12. Found: C, 60.07; H, 10.82; N, 20.88.

The O-dimethylaminopropyl derivative was prepared by adding the free base of hexahydro-1-azepinepropionamidoxime (18.5 g., 0.1 mole) to a cooled solution of freshly prepared sodium ethoxide (from 2.3 g. of sodium and 250 ml. of anhydrous ethanol). To this mixture was added 13.4 g. (0.11 mole) of 3-dimethylaminopropyl chloride and after refluxing for 4 hours the solution was stirred overnight. The ethanol was removed *in vacuo*, ice-water was added to dissolve inorganic salt and the oil was extracted with chloroform. After concentration, the residual oil was fractionated to give 7.3 g. (27%) of an oil, b.p. 45–70° (0.04 mm.), $n^{27}D$ 1.4738.

Anal. Calcd. for $C_{14}H_{30}N_4O$: N, 20.75. Found: N, 20.38.

The dimethiodide melted at 146–149° when recrystallized from ethanol.

Anal. Calcd. for $C_{16}H_{36}I_2N_4O$: N, 10.11; I, 45.82. Found: N, 9.84; I, 46.45.

Reduction of ε-Caprolactam.—Using the procedure described by Brown and Subba Rao,[12] 11.3 g. (0.1 mole) of ε-caprolactam was reduced with sodium borohydride–aluminum chloride in diglyme to give 1.6 g. (16%) of hexahydroazepine, b.p. 137–139°, $n^{27}D$ 1.4628; lit.[21] b.p. 138–138.2°, $n^{23}D$ 1.4654.

The hydrochloride was recrystallized from methanol–petroleum ether, m.p. 235–237°, lit.[21] m.p. 236°. This compound gave no depression of the melting point when mixed with a sample prepared by lithium aluminum hydride reduction of ε-caprolactam.

Hexahydro-1-azepineacetonitrile.—To 65 g. (0.66 mole) of hexahydroazepine in 300 ml. of benzene there was added slowly, with cooling and stirring, 25 g. (0.33 mole) of chloroacetonitrile in 50 ml. of benzene. The solution was refluxed for 1 hour, cooled, filtered and made alkaline with 1 *N* sodium hydroxide solution. The benzene layer was separated, dried, and after concentration *in vacuo*, the residual oil was fractionated to give 18.4 g. (40%) of a colorless oil, b.p. 102–103° (14 mm.), $n^{27}D$ 1.4712.

Anal. Calcd. for $C_8H_{14}N_2$: N, 20.30. Found: N, 19.91.

Hexahydro-1-azepineacetamidoxime Dihydrochloride.—Using the method described for the preparation of hexahydro-1-azepinepropionamidoxime, for a 0.1-mole run, there was obtained 11.93 g. (49%) of white crystals, which had been recrystallized from ethanol, m.p. 171–173° dec.

Anal. Calcd. for $C_8H_{19}Cl_2N_3O$: N, 17.22; Cl, 29.06. Found: N, 16.72; Cl, 28.93.

4-(Hexahydroazepine)-2-butanone.—Hexahydroazepine hydrochloride (33.5 g., 0.25 mole) was dissolved in the minimum amount of methanol (*ca.* 50 ml.) and 100 ml. of acetone was added thereto. If precipitation occurred, sufficient methanol was added to redissolve the solid. Paraformaldehyde (9 g., 0.3 mole) was added and the solution refluxed with stirring for 6 hours. After standing overnight, the solution was filtered and the solvent was removed

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in vacuo; 50 ml. of water was added to the residue and it was made alkaline with 45% aqueous potassium hydroxide. After extraction with ether, the ethereal layer was concentrated and the residual oil fractionated to give 9.9 g. (59%) of a colorless oil, b.p. 87–89° (0.6 mm.), $n^{27}D$ 1.4720.

Anal. Calcd. for $C_{10}H_{19}NO$: C, 71.07; H, 11.33; N, 8.29. Found: C, 70.68; H, 11.46; N, 9.01, 8.82.

The hydrochloride was recrystallized from methanol, m.p. 156–159°.

Anal. Calcd. for $C_{10}H_{20}ClNO$: N, 6.83; Cl, 17.30. Found: N, 6.97; Cl, 17.70.

The oxime was recrystallized from ethanol, m.p. 190–193° as white crystals.

Anal. Calcd. $C_{10}H_{21}ClN_2O$: C, 54.41; H, 9.62; N, 12.69; Cl, 16.06. Found: C, 54.33; H, 9.62; N, 12.89; Cl, 16.07.

2-Acetyl-trimethylene-1,3-bis-(hexahydro-1-azepine Dihydrochloride.—A mixture consisting of 9.2 g. (0.31 mole) of paraformaldehyde, 12.6 g. (0.21 mole) of acetone, 60 ml. of ethanol, 0.5 ml. of concentrated hydrochloric acid and 25 g. (0.18 mole) of hexahydroazepine hydrochloride was refluxed for 1 hour. After this period an additional 6 g. (0.2 mole) of paraformaldehyde was added and the heating was continued for another 2 hours. The mixture then was added to 500 ml. of hot acetone and allowed to cool. The white crystals which separated were recrystallized from ethanol to give 13 g. (20%) of product, m.p. 196–198°.

Anal. Calcd. for $C_{17}H_{34}Cl_2N_2O$: C, 57.84; H, 9.71; N, 7.94; Cl, 20.09. Found: C, 57.49; H, 9.66; N, 7.65; Cl, 19.99.

1-(3-Aminopropyl)-hexahydroazepine Dihydrochloride.—To 8 g. (0.21 mole) of lithium aluminum hydride in 500 ml. of ether, hexahydro-1-azepinepropionitrile (15.2 g., 0.1 mole) in 50 ml. of ether was added slowly. After the addition was completed, the solution was refluxed for an additional hour; 8 ml. of water was added slowly to decompose the excess hydride, this was followed by 6 ml. of 20% aqueous sodium hydroxide and an additional 28 ml. of water. After filtration and washing of the cake with ether, the solvent was removed *in vacuo* to give a yellow oil which was converted to the dihydrochloride with ethanolic hydrogen chloride and was recrystallized from ethanol to give 16.1 g. (70%) of white crystals, m.p. 114–115°.

Anal. Calcd. for $C_9H_{22}Cl_2N_2$: N, 12.23; Cl, 30.97. Found: N, 12.04; Cl, 31.18.

1-(3-Dimethylaminopropyl)-hexahydroazepine Dihydrochloride.—Hexahydroazepine (19.8 g., 0.2 mole) and 3-dimethylaminopropyl chloride (12.15 g., 0.1 mole) in 150 ml. of xylene were refluxed 2.5 hours, then cooled and filtered. The filtrate was gassed with hydrogen chloride and the solid so obtained was recrystallized from ethanol to give 16.72 g. (65%) of white crystalline material, m.p. 272–275°.

Anal. Calcd. for $C_{11}H_{26}Cl_2N_2$: N, 10.90; Cl, 27.59. Found: N, 10.76; Cl, 26.73, 26.83.

1-(2-Dimethylamino-1-methylethyl)-hexahydroazepine dihydrochloride was prepared in the manner described above. It was recrystallized from ethanol and gave white crystals in 70% yield, m.p. 218–220°.

Anal. Calcd. for $C_{11}H_{26}Cl_2N_2$: N, 10.90; Cl, 27.59. Found: N, 10.06; Cl, 27.37.

1-(2-Diethylaminoethyl)-hexahydroazepine dihydrochloride was prepared in the manner described above. It was recrystallized from ethanol and gave white crystals in 72% yield, m.p. 237–240°, lit.[22] m.p. 222–224° dec.

Anal. Calcd. for $C_{12}H_{28}Cl_2N_2$: N, 10.34; Cl, 26.17. Found: N, 10.23; Cl, 26.00.

Ethyl Hexahydro-1-azepinepropionate.—A mixture of 9.9 g. (0.1 mole) of hexahydroazepine and 9 g. (0.05 mole) of ethyl 3-bromopropionate in 100 ml. of benzene was refluxed for 1.5 hours. The solution darkened and precipitation occurred. After cooling, the reaction mixture was extracted with an equal volume of water and the benzene layer dried and then concentrated *in vacuo*. Fractionation of the residual oil gave 9 g. (90%) of the desired product, b.p. 125–132° (14 mm.), $n^{27}D$ 1.4580.

Anal. Calcd. for $C_{11}H_{21}NO_2$: C, 66.39; H, 10.64; N, 7.04. Found: C, 66.35; H, 10.36; N, 7.06.

Hexahydro-1-azepineacetaldehyde.—To a solution of 19.8 g. (0.2 mole) of hexahydroazepine in 400 ml. of benzene was added slowly 10.3 g. (0.1 mole) of 3-chloro-2-hydroxypropionitrile. The solution was refluxed 4 hours, allowed to stand overnight, filtered, concentrated and fractionated to give 8.7 g. (62%) of an oil, b.p. 69–71° (0.2 mm.), $n^{27}D$ 1.4821.

Anal. Calcd. for $C_8H_{15}NO$: C, 68.14; H, 10.72; N, 9.93. Found: C, 67.87; H, 10.59; N, 10.04.

The hydrochloride salt melted at 92–94° with decomposition when recrystallized from ethanol.

Anal. Calcd. for $C_8H_{16}ClNO$: C, 54.13; H, 9.08; N, 7.89; Cl, 19.97. Found: C, 53.08; H, 9.24; N, 8.30; Cl, 20.45.

1-Benzylhexahydroazepine Hydrochloride.—With stirring, 12.6 g. (0.1 mole) of benzyl chloride in 50 ml. of benzene was added to a solution of 19.8 g. (0.2 mole) of hexahydroazepine in 400 ml. of benzene and refluxed for 2 hours. After cooling and filtering, the solution was concentrated and the residual yellow oil was fractionated, b.p. 80–82° (0.5 mm.), and gassed with hydrogen chloride. Recrystallization from ethanol–ether gave 13.7 g. (61%) of white crystalline material, m.p. 163–165°.

Anal. Calcd. for $C_{13}H_{20}ClN$: C, 69.33; H, 8.49; N, 6.22; Cl, 15.56. Found: C, 68.95; H, 8.99; N, 6.13; Cl, 15.50.

(22) F. F. Blicke and E. B. Hotelling, THIS JOURNAL, **76**, 2122 (1954).

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[CONTRIBUTION FROM THE CHEMICAL RESEARCH DEPARTMENT, RESEARCH AND ENGINEERING DIVISION, MONSANTO CHEMICAL CO.]

Polymethine Dyes. I. A Comparison of Several Vinylogous Series in which the Polymethine Chains Are Terminated by Aryl Groups[1]

BY WILLIAM B. TUEMMLER AND BERNARD S. WILDI[2]

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The preparation and absorption spectra of four series of polymethine dyes having polymethine chains terminated by aryl groups are described. By applying principles known from the triphenylmethane- and cyanine dyes, it is possible to identify *x*-, *y*- and *x'*-bands in these spectra. A large bathochromic shift of the *y*-band as well as the *x*-band occurs as conjugation in the chain is extended.

Introduction

The polymethine dyes have provided some of the outstanding examples of the successful correlation of color and constitution in organic molecules. Particularly significant studies in the cyanine field have been reported by Brooker and his colleagues[3]

(1) Presented in part before the Organic Division of the American Chemical Society, 129th Meeting, Dallas, Texas, April 9, 1956.

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(3) (a) L. G. S. Brooker, R. H. Sprague and H. N. J. Cressman, THIS