material was stored in a vacuum desiccator over potassium hydroxide pellets.

Anal. Calcd. for $C_8H_{16}O_4Hg$: C, 25.50; H, 4.28; Hg, 53.24. Found: C, 25.3; H, 4.5; Hg, 54.0.

Preparation of 2-Acetoxymercuri-1-methoxy-1-ethoxyethane.—A solution of 4 g. (0.174 mole) of sodium in 100 cc. of dry methyl alcohol was added dropwise to a solution of 20 g. (0.063 mole) of mercuric acetate in 250 cc. of dry methyl alcohol until a reddish-orange precipitate of the basic salt began to appear. Ethyl vinyl ether was then added dropwise until this precipitate just dissolved. Alternate additions of sodium methoxide and ethyl vinyl ether were made in this manner until further addition of sodium methoxide failed to precipitate the basic salt. The solution was then evaporated to dryness under vacuum. The residue was taken up in chloroform, filtered to remove sodium acetate and the chloroform solution again evaporated under vacuum. The crystalline residue was recrystallized from 30–60° petroleum ether. About 0.5 g. of this product was tested for catalytic activity, and another small portion was dried in vacuum over phosphoric anhydride, m.p. 56–57°.

Anal. Calcd. for $C_7H_{14}O_4Hg$: Hg, 55.30. Found: Hg, 55.97.

The remainder of the product was stored in a tightly-capped bottle in the refrigerator. Examination of this material after about 7 months showed that it had decomposed largely into free mercury and a colorless two-phase liquid. Fractionation of the liquid gave 2 g., b.p. 31–36°, which had a slight odor of acetaldehyde but was mostly wet ethyl vinyl ether, and 6 g., b.p. 46.5–62°, which probably contained dimethyl acetal.

Decomposition of 2-Acetoxymercuri-1,1-diethoxyethane.—A slurry of 60 g. (0.16 mole) of this compound in 300 cc. of *n*-heptane was brought to gentle reflux on an efficient distilling column. An equimolar amount of glacial acetic acid was then added dropwise to this refluxing slurry over a 45-minute period. The solids in the pot turned from a white to a cream color after this addition, and after 1.5 hr. of reflux, the vapor temperature settled at 36°. Slow fractionation gave 3 g. of 94% pure ethyl vinyl ether. Further fractionation gave 22 g. over the range 40–98°, containing 16.5% ethyl vinyl ether and including a large amount of distillate, b.p. 69–70°, which was the azeotrope of ethyl alcohol with *n*-heptane. The total yield of ethyl vinyl ether was therefore 56%. No free mercury appeared during this distillation until the vapor temperature had reached 70°. All attempts to determine the form in which mercury was present in the distillation residue were unsuccessful, but it appeared that no simple salts of mercury were formed.

PHILADELPHIA 37, PENNA.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ROHM & HAAS CO.]

Homogeneous Metal Salt Catalysis in Organic Reactions. II. The Reaction of Vinyl Ethers with Aminoalcohols and 1,2-Diamines

BY WARREN H. WATANABE

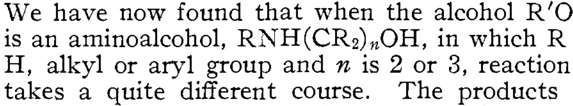
RECEIVED NOVEMBER 2, 1956

When aminoalcohols, $RNH(CR_2)_nOH$, in which R is H, alkyl or aryl and n is 2 or 3, are treated with alkyl vinyl ethers in the presence of mercuric salts of weak acids or silver salts such as silver nitrate or silver acetate, there are formed in good yield 2-methyloxazolidines (I, $n = 2$) or 2-methyltetrahydro-1,3-oxazines (I, $n = 3$). Similarly, 1,2-diamines, treated with alkyl vinyl ethers with the same catalysts, give 2-methylimidazolidines (II). These new reactions are improved methods of preparation of these relatively unstable compounds. The relation of these reactions to vinyl transetherification[1] is discussed and a mechanism is proposed.

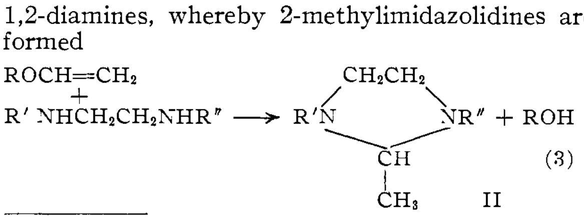
In a previous publication we have described a method of preparation of vinyl ethers by the reaction

$$ROCH{=}CH_2 + R'OH \rightleftarrows ROH + R'OCH{=}CH_2 \quad (1)$$

which is catalyzed by mercuric salts of weak acids.[1] We have now found that when the alcohol R'OH is an aminoalcohol, $RNH(CR_2)_nOH$, in which R is H, alkyl or aryl group and n is 2 or 3, reaction 1 takes a quite different course. The products in these instances are 2-methyloxazolidines (I, $n = 2$) or 2-methyltetrahydro-1,3-oxazines (I, $n = 3$) rather than the vinyl ethers


(2)

We have been able also to extend this reaction to 1,2-diamines, whereby 2-methylimidazolidines are formed



The yields of the cyclic compounds prepared by this method range from about 40 to greater than 80% and are limited largely by the stability of these compounds. This new reaction thus is a simple, useful and generally preferable alternative to the standard method of preparation of I and II, which is by reaction of the aminoalcohols[2] or diamines[3] with acetaldehyde.

Catalysts.—The same catalysts found to be effective in our previous study of vinyl transetherification (*i.e.*, mercuric salts of carboxylic acids[1]) were also the most efficient catalysts for the present reaction. It was of interest that mercuric sulfate, which is a very active catalyst for vinyl transetherification at very low temperatures,[4] had no activity for reaction 2 and, probably due to the strongly basic nature of the reaction mixture, had no effect at all on the vinyl ether. Moreover, in contrast to the vinyl transfer reaction 1, for which mercuric salts are highly specific catalysts, the present reaction also was found to be catalyzed by silver nitrate and silver acetate. Zinc acetate,

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[1] W. H. Watanabe and L. E. Conlon, THIS JOURNAL, **79**, 2828 (1957).

(2) (a) E. D. Bergmann, *Chem. Revs.*, **53**, 309 (1953); (b) L. Knorr and H. Matthes, *Ber.*, **34**, 3484 (1901); (c) A. I. Kiprianov and B. A. Rashkovan, *J. Gen. Chem.* (*U.S.S.R.*), **7**, 1026 (1937); *C. A.*, **31**, 5356 (1937); (d) N. K. Ushenko, *C. A.*, **37**, 4395 (1943); (e) E. Zimkin and E. D. Bergmann, *Rec. trav. chim.*, **71**, 229 (1952).

(3) (a) J. Th. L. B. Rameau, *ibid.*, **57**, 192 (1938); (b) G. Lob, *ibid.*, **55**, 859 (1936); (c) V. S. Salvin and J. R. Adams, U. S. Patent 2,546,169 (March 27, 1951).

(4) R. L. Adelman, THIS JOURNAL, **77**, 1669 (1955).

TABLE I

PRODUCTS PREPARED BY REACTIONS 2 AND 3

Aminoalcohol or diamine	R in $ROCH=CH_2$	Product[a]	B.p. or m.p. product °C.	Mm.	Method	Catalyst	Crude yield, %	Pure yield, %
Ethanolamine	2-Butoxyethyl	2-Methyl-ox.	50–55	60	A	$Hg(OBz)_2$	55	. .
1-Aminopropanol-2	2-Butoxyethyl	2,5-Dimethyl-ox.	62.5–64.5	100	A	$Hg(OBz)_2$	53	40
2-Aminobutanol-1	2-Butoxyethyl	2-Methyl-4-ethyl-ox.	63–66	40	A	$Hg(OBz)_2$	64	55
2-Amino-2-methyl-propanol-1	2-Butoxyethyl	2,4,4-Trimethyl-ox.	70.5–71	120	A	$Hg(OBz)_2$	83	72
	Ethyl	2,4,4-Trimethyl-ox.	70.5–71	120	B	$Hg(OAc)_2$	. .	14
N-Methylethanolamine	Vinoxyethyl	2,3-Dimethyl-ox.	54–55	120	A	$Hg(OAc)_2$	. .	68
N-Methylethanolamine	Vinoxyethyl	2,3-Dimethyl-ox.	54–55	120	A	$AgNO_3$	. .	22
N-Methylethanolamine	Vinoxyethyl	2,3-Dimethyl-ox.	54–55	120	A	AgOAc	. .	32
N-Phenylethanolamine	Ethyl	2-Methyl-3-phenyl-ox.	M. 58.5–59		B	$Hg(OAc)_2$	85	64
3-Amino-1-propanol	2-Butoxyethyl	2-Methyl-tet.	68.5–69	100	A	$Hg(OBz)_2$	. .	65
3-Amino-1-propanol	Ethyl	2-Methyl-tet.	68.5–69	100	B	$Hg(OAc)_2$	. .	60
Ethylenediamine	Ethyl	2-Methyl-imid.	M. 47.5–48.5		B	$Hg(OBz)_2$	41	. .
N,N'-Diphenylethylene-diamine	Ethyl	2-Methyl-1,3-diphenyl-imid.	M. 92–93.5		B	$Hg(OAc)_2$	82	66

[a] For ox. read oxazolidine; for tet. read tetrahydro-1,3-oxazine; for imid., read imidazolidine.

cadmium acetate, cuprous chloride and ammonium chloride were found, under our testing conditions, to be without activity. The mercury salts were, however, preferable to the silver salts, because the latter underwent more extensive decomposition, accompanied by rapid loss in catalyst activity.

Reaction Procedures.—In Table I there are listed the compounds which have been prepared by reactions 2 and 3. The alkyl vinyl ethers used were those conveniently available and readily separable from the products of reaction. Catalysts generally used were mercuric acetate or mercuric benzoate; silver acetate and silver nitrate were tested in single reactions solely to demonstrate their activity.

Of the two methods used to carry out reaction 2, the more useful was the one in which the product was removed by distillation from the reaction mixture as rapidly as it was formed. Continuous removal was of particular advantage in that 2-methyloxazolidines (or the tautomeric Schiff bases, in the case of compounds I where R' = H) are rapidly converted to condensation products at elevated temperatures.[5] This procedure (method A in Table I) is possible since 2-methyloxazolidines and 2-methyltetrahydro-1,3-oxazines have boiling points lower than their parent aminoalcohols. By choice of a high-boiling vinyl ether as the vinyl ether component, a system usually can be devised such that the lowest-boiling component will be the product, which can then be removed rapidly by distillation. Yields by this method are indeed to a large extent determined by the efficiency and speed at which this separation can be effected. It is certainly this possibility of continuous rapid removal of product which results in higher yields by this reaction than from the alternative method of preparation from acetaldehyde, in which the product cannot be removed until reaction is complete.

This distillation method loses its utility, however, when the product is very high-boiling (*e.g.*, 2-methyl-3-phenyloxazolidine), since an even higher-boiling vinyl ether would have to be employed. Fortunately, the phenyl compound proved to be relatively stable and could thus be obtained in good yield by heating the reactants under reflux (method B in Table I). The reflux procedure also was used in the preparation of 2-methylimidazolidines since the boiling points of these compounds are almost identical with those of the starting diamines, and the products cannot therefore be separated by distillation. Separation by crystallization could, however, be effected, since the imidazolidines had melting points higher than those of the starting diamines.

Discussion

A point of particular interest in the present work is the problem of whether reactions 2 and 3 proceed in a single step, or in two discrete steps, with a vinyl compound as an intermediate. There are substantial arguments for both hypotheses, but we believe that the preponderance of present evidence is in favor of a single-step mechanism. In support of a two-step mechanism are these points: (1) It already has been shown that mercuric salts of weak acids will catalyze vinyl transetherification.[1] It also has been found that aminoalkyl vinyl ethers can be cyclized by both mercuric and silver salts to oxazolidines and tetrahydro-1,3-oxazines.[6] Thus the two possible separate steps of a two-step mechanism (vinyl transetherification, followed by cylization) are known reactions. (2) We moreover estimate, from the relative amounts of catalyst required for a sensible rate of reaction at room temperature, that cyclization proceeds much more rapidly than vinyl transetherification. Thus the exclusive isolation of the cyclic product is consistent with the probable relative rates of the presumed two steps.

Arguing against a two-step mechanism, however, are the following points: (1) the rate of the over-all reaction 2 or 3 is estimated, again purely on the basis of relative amounts of catalyst required for reasonable rates at room temperature, to be greater by at least a factor of five than vinyl trans-

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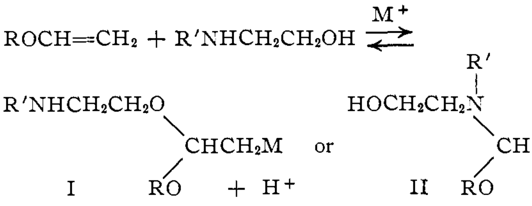
[5] W. S. Emerson, S. M. Hess and F. C. Uhle, THIS JOURNAL, **63**, 872 (1941), have shown that aliphatic Schiff bases undergo aldol-type condensations, splitting off amine. H. R. Nace and E. P. Goldberg, *ibid.*, **75**, 3646 (1953), conclude from infrared evidence that 2-propyl-4-ethyloxazolidine, which polymerizes and changes rapidly in refractive index on standing, does so through an aldol-type condensation.

[6] W. H. Watanabe, unpublished work.

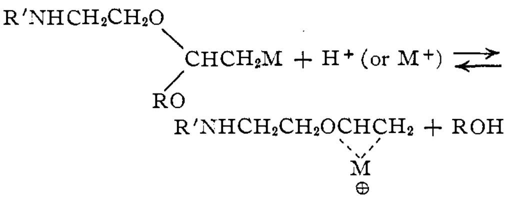
etherification. If this is the case, the transetherification cannot then be an intermediate step. (2) The two-step mechanism does not accommodate the 1,2-diamine reaction (3), unless an –O–vinyl to –NH transfer can occur. There is no reported reaction of such a type. (3) The two-step mechanism does not accommodate silver salt catalysis, since it has been found that silver salts do not catalyze vinyl transetherification.[1]

A possible one-step mechanism would be the following, which is patterned closely after our earlier suggested path for vinyl transetherification

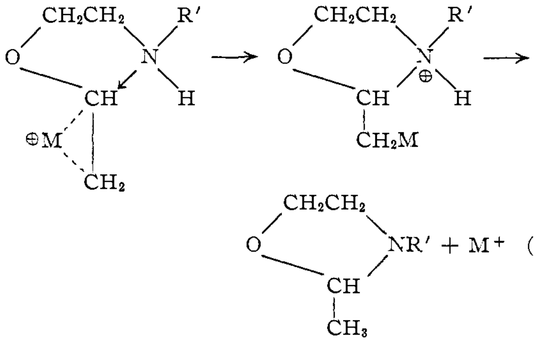


(4a)

where $M^+ = HgOAc^+$ or Ag^+. For the case of I



(4b)



(4c)

A similar intramolecular displacement can be written for II. We are, however, much less satisfied with the above postulate of a stable intermediate I or II in this reaction than in the case of vinyl transetherification where a similar intermediate was proposed, since essentially all of the metal salt should be complexed with the amine, leaving little available for covalent metal–carbon bond formation. It is nevertheless necessary that the metal salt in some manner activate the formation of a new O–C bond and, in lieu of a more sturdy alternative, we suggest reaction through such intermediates as I or II. It is, of course, possible that the steps (4a-c) take place simultaneously, in a single concerted process, obviating the necessity for the formation of any long-lived intermediates.

Experimental

Materials.—The aminoalcohols and diamines used were commercially available materials and were redistilled or recrystallized before use. 1,2-Divinoxyethane was prepared by the base-catalyzed reaction of acetylene with ethylene glycol.[7] The other vinyl ethers were commercially available and were purified by distillation. The metal salts were reagent grade chemicals, used as received.

General Comments.—Those compounds prepared where R = H and $n = 2$ in I (no substitution on the nitrogen of the 2-methyloxazolidines) were, with the exception of 2,4,4-trimethyloxazolidine, relatively unstable substances which became viscous upon standing, even in the cold.[5,8] There was thus an unavoidable loss upon the redistillation of the first crude product, and yields are therefore given for both the crude and redistilled product. As one consequence of the instability of these compounds, both n^{25}_{D} and d^{25}_{4} values changed rapidly with time, and while every attempt was made to measure these values as quickly as possible, not too much reliance should be placed on these constants. Those compounds with N-substitution, or when $n = 3$, were much more stable, and the constants reported for them are more reliable. However, these substances will also darken and decompose slowly if left at room temperature.

Catalyst Testing.—The reaction of N-methylethanolamine and 1,2-divinoxyethane, which with mercuric acetate as catalyst gives about a 70% yield of 2,3-dimethyloxazolidine, was used as the standard reaction for the testing of various metal salts for catalytic activity. By this test mercuric acetate, mercuric benzoate, silver nitrate and silver acetate were found to be active, and mercuric sulfate, cuprous chloride, zinc acetate, cadmium acetate and ammonium chloride were found to be inactive. Recoveries of 1,2-divinoxyethane from tests on inactive substances ranged from 89 to 99% (recovery from the mercuric sulfate run, 99%).

Preparation of 2,5-Dimethyloxazolidine.—A cloudy, two-phase mixture resulted when 1-aminopropanol-2 (77.1 g., 1.03 moles) was mixed with 2-butoxyethyl vinyl ether (171.9 g., 1.19 moles). When 1 g. of mercuric benzoate was added, however, and dissolved by vigorous shaking, the mixture became homogeneous and an exotherm resulted which quickly brought the temperature of the solution to about 50°. The solution was therefore cooled and placed on a distillation column. An initial product cut, b.p. 55–68.5° (100 mm.), was taken, the distilling flask cooled and 1 g. of mercuric benzoate added to the reaction mixture; a second product cut taken at 65.5–70° (100 mm.) and the flask again cooled and another 1 g. of mercuric benzoate added; and a final product cut taken at 66–67°/100 mm. The weight of combined crude product was 55.1 g., a crude yield of 53%. Continued distillation of the reaction mixture yielded 117.6 g. of 2-butoxyethanol, b.p. 72–75° (20 mm.), 61–61.5° (10 mm.), a yield based on the aminoalcohol of 97%. The crude product was redistilled, giving 34.0 g. of pure 2,5-dimethyloxazolidine, b.p. 62.5–64.5° (100 mm.), n^{25}_{D} 1.4366, d^{25}_{4} 0.9371, which was thus obtained in 33% yield.

Anal. Calcd. for $C_5H_{11}ON$: C, 59.37; H, 10.96; N, 13.85. Found: C, 59.94; H, 11.36; N, 13.75.

2-Methyl-4-ethyloxazolidine was prepared by essentially the same method: n^{25}_{D} 1.4407, d^{25}_{4} 0.9219. *Anal.* Calcd. for $C_6H_{13}ON$: C, 62.57; H, 11.37; N, 12.16. Found: C, 62.70; H, 11.28; N, 11.85.

2,3-Dimethyloxazolidine was also prepared in a similar manner: n^{25}_{D} 1.4200, d^{25}_{4} 0.9001. *Anal.* Calcd. for $C_5H_{11}ON$: C, 59.37; H, 10.96; N, 13.85. Found: C, 59.38; H, 10.74; N, 13.77.

2,4,4-Trimethyloxazolidine.—This was prepared by both methods A and B: n^{25}_{D} 1.4240, d^{25}_{4} 0.8904. *Anal.* Calcd. for $C_6H_{13}ON$: C, 62.57; H, 11.37; N, 12.16. Found: C, 62.82; H, 11.49; N, 12.04.

The infrared spectrum of the product was determined and showed that this material was identical with 2,4,4-trimethyloxazolidine, prepared otherwise by the reaction of acetylene with 2-amino-2-methylpropanol-1.[9] There was no absorption in the double bond region, indicating first, that there was less than 0.5% of a vinyl ether present and, second, that this compound must exist entirely in the cyclic form and not as a Schiff base. This lack of any appreciable amount of a Schiff base tautomer is probably the reason why this compound is so much more stable than the other oxazolidines (I), with R = H, which we have prepared, and which all show evidence of existing at least partially in the Schiff base form.[8] The lack of vinyl ether is particularly signifi-

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[7] W. Reppe, U. S. Patent 1,959,927 (May 22, 1934); A. E. Favorskii and M. F. Shostakovskii, *J. Gen. Chem.* (*U.S.S.R.*), **13**, 1 (1943); *C. A.*, **38**, 330 (1944).

[8] *Cf.* A. M. Paquin, *Ber.*, **82**, 316 (1949).

[9] W. H. Watanabe and L. E. Conlon, THIS JOURNAL, **79**, 2825 (1957).

cant, since both the oxazolidine and the isomeric vinyl ether have identical boiling points[9] and no fractionation could have occurred by distillation if both these compounds had been formed in the reaction. Moreover, if the reaction proceeds in two steps, then the presumed first step (vinyl transetherification) would not be appreciably hindered sterically, whereas the presumed second step (cyclization) should be seriously hindered. Thus, this example is a particularly favorable case for isolation of the vinyl ether if any had formed.

2-Methyltetrahydro-1,3-oxazine was prepared by both methods A and B: $n^{25}\mathrm{D}$ 1.4407, d^{25}_4 0.9459. *Anal.* Calcd. for $C_5H_{11}ON$: C, 59.37; H, 10.96; N, 13.85. Found: C, 59.57; H, 11.00; N, 13.59.

Preparation of 2-Methyl-3-phenyloxazolidine.—N-Phenylethanolamine (141.5 g., 1.03 moles) was dissolved in 86.3 g. (1.20 moles) of ethyl vinyl ether and 1 g. of mercuric acetate added to this solution. The solution warmed spontaneously and began to boil before all the mercuric salt had gone into solution. It was immediately placed under a reflux condenser and heated under reflux for 2 hr. During this period, the reaction temperature rose from 45 to 78°. The reaction mixture was then poured into a beaker and chilled in ice, whereupon it set to a crystalline mass. The solid was removed by filtration and recrystallized from ethyl alcohol, giving 143.8 g. of 2-methyl-3-phenyloxazolidine, m.p. 58–59°, a yield of 85.5%. This product was recrystallized again from 30–60° petroleum ether, resulting in 107.5 g. of pure product (64% yield), m.p. 58.5–59°. A final recrystallization from 85–100° petroleum ether gave an analytical sample, m.p. 59–59.5° (lit.[2e] 60.5–61°).

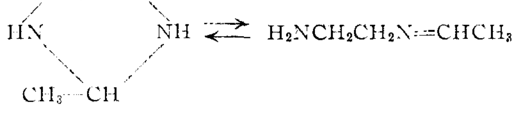
Anal. Calcd. for $C_{10}H_{13}ON$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.62; H, 7.89; N, 8.54.

Preparation of 2-Methylimidazolidine.—Ethylenediamine (65.5 g., 1.09 moles) was dissolved in 133.5 g. (1.85 moles) of ethyl vinyl ether and 1 g. of mercuric benzoate added to this solution. The mercuric salt dissolved only partially even with vigorous shaking; there was no immediate exotherm. The mixture was then heated under reflux for 8 hr. During this period the pot temperature rose from 42 to 51°, and almost all of the mercuric salt went into solution, accompanied by the formation of some globules of mercury. The solution was cooled and left overnight at room temperature. On the following day another 1 g. of mercuric benzoate was added. This time the mercuric salt went rapidly and completely into solution. Reflux was resumed, and over a 1-hr. period the pot temperature rose from 51.5 to 60°. The solution was then cooled and flash-distilled at about 0.5 mm. pressure into a receiver cooled with Dry Ice–acetone. The first cut of this flash-distillation, 66.9 g., was obtained without heating the distilling flask; this cut was terminated when a solid material started to plug the outlet of the take-off tube. A wide-bore outlet was then utilized, and a second cut was taken by heating the distilling flask to a maximum liquid temperature of 73°. This second fraction, 107.7 g., was partly solid at room temperature, but the solid soon dissolved in the liquid portion. The residue weighed 18.1 g.

The second fraction was overlaid with about twice its volume of 100–140° petroleum ether, well shaken, and chilled in Dry Ice–acetone to induce crystallization. The crystals were filtered under nitrogen from the resultant two-phase liquid mixture. The filtrate was again chilled, and the solid which formed again filtered off under nitrogen. This procedure was repeated about six times until no further crystallization occurred. The combined solid product was dried under vacuum at room temperature. The yield of this once-crystallized product, m.p. 46–49°, was 38.4 g., 41% based on the diamine. This material was recrystallized out of 30–60° petroleum ether to obtain an analytical sample, which was a white, very volatile, hygroscopic solid, m.p. 47.5–48.5°. Potentiometric titration of this sample with standard 0.1 *N* HCl gave replicate values of 43.39 and 42.91 for the neutralization equivalent (theor. for 2-methylimidazolidine, 43.07). Elementary analysis was found to be very difficult because of the hygroscopicity and volatility of the material, and an analysis for nitrogen could not therefore be obtained.

Anal. Calcd. for $C_4H_{10}N_2$: C, 55.77; H, 11.70; N, 32.53. Found: C, 56.36; H, 11.57.

The infrared spectrum of this compound showed bands at 1670 cm.$^{-1}$ attributable to —C=N— stretching, and at 1595 cm.$^{-1}$, probably due to -NH_2 deformation. These results are consistent with the Schiff base form of the imidazolidine



Preparation of 2-Methyl-1,3-diphenylimidazolidine.—N,N′-Diphenylethylenediamine (100.9 g., 0.48 mole) was shaken vigorously with 72.0 g. (1.0 mole) of ethyl vinyl ether, but only a small part of the solid diamine dissolved. One gram of mercuric benzoate was dissolved in this mixture, and a strong exotherm then resulted. The mixture was immediately placed under reflux and heating applied when the initial exotherm subsided. After 21 min. of reflux almost all of the solid had gone into solution and the liquid temperature had risen from 35.5 to 49°. Almost immediately thereafter crystallization suddenly occurred, filling the flask with solid and lowering the liquid temperature to 42°. After a further 40 min. of reflux, the mixture was cooled and the solid product dried under vacuum. Part of this solid was recrystallized from methanol, m.p. 90–91.5°, and the remainder from 85–100° petroleum ether, m.p. 91.5–95°. The total yield of recrystallized product was 93.4 g., 82% based on the diamine. This product was further recrystallized out of methanol, giving 75 g. (66% yield) of pure 2-methyl-1,3-diphenylimidazolidine, m.p. 92–93.5° (lit.[3c] 98–100°), ebulliometric molecular weight, 226 (theor. 238).

Anal. Calcd. for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.76. Found: C, 80.40; H, 7.47; N, 11.76.

PHILADELPHIA 37, PENNA.

[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Synthetic Hypotensive Agents. V. 4-(2′-Aminoethyl)-piperidine Derivatives

BY ARTHUR P. PHILLIPS

RECEIVED DECEMBER 19, 1956

A series of 4-(2′-aminoethyl)-piperidines has been prepared for testing for hypotensive ganglionic blocking activity. The most active compound in the series was comparable in activity to hexamethonium.

Following the discovery[1,2] of ganglionic blocking activity in 1-methyl-3-(4′-dimethylaminobutyl)-piperidine (I) and its bis-quaternary ammonium salts, several series of compounds[3] modelled after I have been prepared and tested for this kind of activity. The present paper reports the preparation and properties of another series of compounds structurally related to I. These are some 4-(2′-aminoethyl)-piperidine derivatives which can be represented by the general formula II. The products were made by the sequence of reactions shown in Fig. 1.

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(1) S. Norton and A. P. Phillips, *Nature*, **172**, 867 (1953).

(2) A. P. Phillips, THIS JOURNAL, **76**, 2211 (1954).

(3) Paper IV of this series, A. P. Phillips, *ibid.*, **78**, 1930 (1956).