Cyclic Guanidines. X.\textsuperscript{1} Synthesis of 2-(2,2-Disubstituted Ethenyl- and Ethyl)-2-imidazolines as Potent Hypoglycemics\textsuperscript{2}

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2-(2,2-Disubstituted ethenyl- and ethyl)-2-imidazoline derivatives (11, 14) were prepared by direct cyclization of active intermediates, 3,3-disubstituted acrylimidic ethyl esters (9, 10), with ethylenediamine. The stereoisomers, (Z)- and (E)-3-phenyl-3-pyridylacrylic acid esters (6c–e), nitriles (7c–e) and amides (8c–e), as well as (Z)- and (E)-3-phenyl-3-pyridylacrylic acid esters (10c–e), and (Z)- and (E)-2-(2-pyridylethynyl)-2-imidazolines (11c–e), were isolated. Their structures are discussed. Compounds 11 and 14 showed potent hypoglycemic activity.

Keywords—2-(2,2-disubstituted ethenyl)-2-imidazoline; 2-(2,2-disubstituted ethyl)-2-imidazoline; Wittig-Horner reaction; stereoisomers of 3,3-disubstituted acrylic acid derivatives; hypoglycemic activity

We have reported that monocyclic guanidines and related compounds having a bulky group showed potent hypoglycemic activity.\textsuperscript{4} 2-Imidazolines substituted with a bulky group at position 2, such as 2-(x-ethoxybenzyl),\textsuperscript{5} 2-(x-hydroxybenzhydryl),\textsuperscript{6} and 2-(2-phenylpropyl)-2-imidazoline,\textsuperscript{7} are also potent hypoglycemics. The structure-activity relationships in the cyclic guanidines and 2-imidazoline derivatives suggested that a bulkyl group located at a distance of one or two carbon units from position 2 in the imidazole ring is important for hypoglycemic activity. We also reported in the preceding paper\textsuperscript{4b} that a tricyclic guanidine structure having a benzene ring in the bulky group coplaner with the imidazole ring generally resulted in potent activity. This paper deals with the synthesis and biological activity of 2-(2,2-disubstituted ethenyl- and ethyl)-2-imidazoline derivatives.

A few 2-(2-monosubstituted ethenyl)-2-imidazoline derivatives have been synthesized by the reaction of 2-methyl-2-imidazoline with arylaldehydes\textsuperscript{8} and by the cyclization of 2-thienylacrylimidic ester with ethylenediamine.\textsuperscript{8}

3,3-Disubstituted acrylic acid derivatives, the ethyl esters (6), nitriles (7), and amides (8), were prepared from the phenyl ketone derivatives (1) with the diethyl phosphonoacetic acid derivatives (2, 3, 4), respectively, in the presence of sodium ethoxide in ethanol in good yield by Webb's modified Wittig-Horner reaction.\textsuperscript{9} The pyridine-substituted compounds

\textsuperscript{1} Part IX: F. Ishikawa, Y. Watanabe, and J. Saegusa, Chem. Pharm. Bull., 28, 1357 (1980); This paper is regarded as 10th report in our series on cyclic guanidines since the nature of the compounds described in this paper is analogous to that of the cyclic guanidines.

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\textsuperscript{3} Location: 1-16-13 Kidakasai, Edogawa-ku, Tokyo 132, Japan.


\textsuperscript{5} A.C. White and R.M. Black, Ger. Offen. 2257784 (1973) [Chem. Abstr., 79, 78833 (1973)].

\textsuperscript{6} H. Roebke, Japan Kokai Tokkyo Koho 76143668 (1976).


6c—e, 7c—e, and 8c—e were isolated as a mixture of the (Z)- and (E)-isomers. Among them the amides (8c—e), the 2-pyridyl-substituted ester (6c), and the nitrile (7c) could be separated into the (Z)- and (E)-isomers by silica gel chromatography or recrystallization. The Z: E formation ratios of the reaction products were determined by nuclear magnetic resonance (NMR) spectroscopy or high performance liquid chromatography (HPLC).

Heating the acrylic acid esters (6) or the nitriles (7) with ethylenediamine at 200° or higher temperatures did not give 2-ethylene-2-imidazolines (11). An attempt to prepare the active acrylimidic acid ester (10) from the nitrile (7) by treatment with ethanolic hydrogen chloride also failed.

Reaction of 7a, b with feric chloride in isopropyl chloride followed by treatment with ethanol gave the corresponding ethyl N-isopropylacrylimidate (9a, b) in good yield by a modification of Jolivet's method\(^{10}\) in which acrylonitrile was converted via the nitrilium salt to 2-propenyl amidines. Compound 9a or 9b readily reacted with ethylenediamine at 100—140° to give the desired 2-ethenyl-2-imidazoline derivative (11a or 11b). However, the pyridine-substituted compounds 7c—e did not yield the nitrilium salts because of the prior reaction of the pyridine base with feric chloride.

Reaction of 3,3-diphenylacrylamide (8b) with the Meerwein reagent afforded the imidic ethyl ester (10b) as an oil in good yield. In the same way, although the free bases of pyridine-substituted derivatives (8c—e) did not yield the imidic ethyl esters (10c—e), the hydrochlorides of (Z)- and (E)-8c—e (except for (Z)-8c) formed (Z)- and (E)-10c—e respectively. Compound

![Chemical diagram](chart1.png)

Equations are as follows:

R: a = Me; b = H; c = CH$_3$; d = CH$_2$CH$_3$; e = CH$_2$CH$_2$N

A = 2NaOEt; B = HCl/H$_2$O; C = 3NaOEt; D = (CF$_3$CO)$_2$O/CH$_3$H$_2$N; E = 4NaOEt; F = H$_2$SO$_4$/AcOH; G = 1. FeCl$_3$; 2. H$_2$O; H = H$_2$NCH$_2$CH$_2$NH$_2$; I = Et$_3$OBF$_4$; J = H$_2$NCH$_2$CH$_2$NH$_2$; K = 5NaOEt; L = H$_2$/Pd-C; M = NaBH$_4$; N = H$_2$NCH$_2$CH$_2$NH$_2$; O = H$_2$NCH$_2$CH$_2$NH$_2$; TsOH; P = H$_2$/Pd-C.

**Chart 1**

(Z)-8c reacted with the Meerwein reagent to give the reaction complex which decomposed to a resin on treatment with sodium bicarbonate solution for the isolation of (Z)-10c. Gentle heating of the imidic ethyl esters (10) with ethylenediamine readily gave the interesting 2-ethynyl-2-imidazoline derivatives (11).

The reaction of phenyl ketones (1) with 2-diethylphosphonomethyl-2-imidazole (5) reported recently by Shiskin et al.\textsuperscript{11} was attempted. Benzoyl pyridines (10c–e) readily gave mixtures of the (Z)- and (E)-isomers of 11c–e on treatment with 5 at room temperature. However, separation of the isomers was difficult. On the other hand, reaction of the phenyl ketones (1a, b) with 5 did not proceed at room temperature and 11a, b were obtained after prolonged heating in poor yield. It appears that compound 5 is rather unreactive in the Wittig-Horner reaction.

Pure (Z)- and (E)-isomers of 8c–e were treated with trifluoroacetic anhydride in the presence of pyridine in dioxane at room temperature\textsuperscript{12} to give the (Z)- and (E)-isomers of 7c–e, respectively. Each isomer of 6c–e was also prepared from the corresponding isomer of 10c–e by heating in aqueous ethanol.

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\textsuperscript{a} C: CDCl\textsubscript{3}, D: DMSO-d\textsubscript{6}.

The structures of the (Z)- and (E)-isomers of 2-pyridylsubstituted derivatives (6c, 7c, 8c) were confirmed on the basis of their NMR spectra. The chemical shift of the methine proton of the (E)-isomer is shifted 0.4–0.8 ppm to lower field in comparison with that of the (Z)-isomer, as shown in Table I, because of the anisotropy effect of the neighboring pyridine nitrogen atom. On the other hand, in the cases of the 3- and 4-pyridyl-substituted compounds no significant difference was observed in the chemical shift of the methine proton on the two isomers. Therefore, the structures were finally determined by X-ray analysis, as shown in Fig. 1.\textsuperscript{13}

\textsuperscript{13} K. Yamazaki, R. Moroi, and M. Sano: Details will be reported elsewhere.
NMR signal positions of the phenyl and methine protons of the (Z)- and (E)-isomers of 6c—e, 7c—e, 8c—e, 10c—e, and 11c—e are listed in Table I. In the cases of the (E)-isomers of the esters (6), imidic acid esters (10), and imidazoline derivatives (11), the signals of phenyl protons are observed as multiplets because of the anisotropy effect of the carbonyl or imino group.\textsuperscript{14} In the case of the (Z)-isomer, the phenyl protons are observed as a singlet. In the nitrile derivatives (7), the singlet signals of phenyl protons in the (E)-isomers are shifted to lower field as compared to the multiplet signals of the (Z)-isomers. The signals of the (Z)-and (E)-isomers of the amide derivatives (8) are observed as multiplets in hexadeuterodimethylsulfoxide.

Catalytic hydrogenation with palladium-charcoal (Pd-C) of 6 gave the ethyl 3,3-disubstituted propionate (12) in good yield. Heating 12 with ethylenediamine at 200° or higher temperatures afforded 2-(2,2-disubstituted ethyl)-2-imidazolines (14) in moderate yield. The hydrogenation of nitriles (7a,b) also gave the propionitriles (13a,b) in good yield, while 7c—e

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\textsuperscript{Dose: 25 mg/kg, p.o.}

did not form the corresponding nitriles (13c–e) under the same conditions. However, heating 7c–e with excess sodium borohydride in ethanol gave the nitriles (13c–e). Reaction of 13a,b with ethylenediamine monosoylinate at 140–160° yielded 14a,b, while 13c–e formed 14c–e only at 220° or higher temperatures. Compounds 14a–e were also easily obtained by catalytic hydrogenation of the 2-ethenyl-2-imidazole derivatives (11).

Hypoglycemic activity was determined in normal fasted rats and the results are shown in Table II. Most of the compounds (11 and 14) were effective. The compounds having a bulkier groups, a phenyl or pyridyl rather than a methyl group, had more potent activity. The difference of activity among phenyl and 2-, 3-, and 4-pyridyl groups was small. Replacement of an ethyl group with ethynyl as a 2-substituent had little effect on the activity. 2-[2-Phenyl-2-(2-pyridyl)ethyl]-2-imidazole (14c), which showed the highest hypoglycemic activity, the highest inhibitory effect against human blood platelet aggregation induced by epinephrine, and the lowest toxicity, was selected for further study from among the 2 substituted-2-imidazole derivatives. Its pharmaceutical profile will be reported elsewhere.

Experimental

All melting points are uncorrected. IR spectra were recorded with a Hitachi 285 spectrometer, and NMR spectra were taken with a Hitachi Perkin-Elmer R-20B5 (60 MHz) or a Varian EM-360 (60 MHz) spectrometer with tetramethylsilane as an internal standard (0 value). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. HPLC were carried out on a Kyowa Seimitsu K-880-D machine. For column chromatography, silica gel (Merck, 0.05–0.2 mm) was used.

Determination of the Z: E Ratio—After work-up in the manner described below, the NMR spectra of the crude reaction products were taken in CHCl₃ or DMSO-d₆. The methine regions were integrated three times and the average values were used to determine the Z: E ratio.

HPLC separation of 8c–e was carried out on the K-880-D HPLC machine using a TSK-Gel LS-100 column, with 4% MeOH-CHCl₃ 4 a flow rate of 1.0 ml/min. Retention times were: 8c; Z 295 sec, E 204 sec. 8d; 145 sec, E 279 sec; Z 497 sec, E 302 sec.

Reaction A. Ethyl 3-Phenyl-3-(2-pyridyl)acrylate (6c) — An ice-cold solution of 2.30 g (0.1 mmol) of Na metal in 75 ml of EtOH was treated with 22.4 g (0.1 mmol) of 2 and stirred at 5–10° for 10 min. Next, 16.5 g (0.09 mol) of 1c was added. After stirring at room temperature for 1 hr, the mixture was refluxed for 2 hr and concentrated in vacuo. The mixture was treated with H₂O and extracted with Et₂O. The extract was washed with H₂O, dried, and concentrated in vacuo. The residual oil was distilled to give 21.2 g (93%) of a mixture of the (Z)- and (E)-isomers of 6c. The mixture (5.0 g) could be separated by column chromatography on silica gel (200 g). The CHCl₃ eluate gave 2.36 g of the (Z)-isomer and 2.24 g of the (E)-isomer.

Compounds 6a, b, d, e were obtained from 1a, b, d, e, respectively, in a similar manner. The results are shown in Table III.

Reaction B. (Z)-Ethyl 3-Phenyl-3-(4-pyridyl)acrylate [Z]-6e — A mixture of 0.13 g (0.5 mmol) of (Z)-10c and 0.3 ml of conc. HCl in 2 ml of EtOH was heated at 50–55° for 2 hr, then concentrated in vacuo. The residue was mixed with 10 ml of satd. NaHCO₃ solution and extracted with Et₂O. The extract was concentrated in vacuo to give 0.12 g (92%) of (Z)-6e, mp 100–102°.

Other experimental results are shown in Table III.

Reaction C. 3-Phenyl-3-(2-pyridyl)acrylonitrile (7c) — An ice-cold solution of 2.3 g (0.1 mol) of Na metal in 75 ml of EtOH was treated with 17.7 g (0.1 mmol) of 3 and stirred at 5–10° for 10 min. Next, 16.5 g (0.09 mol) of 1c was added. After stirring at room temperature for 1 hr, the reaction mixture was heated at 50–60° for 1 hr and then concentrated in vacuo. The residue was treated with H₂O and extracted with H₂O. The extract was washed with H₂O, dried, and concentrated in vacuo. The residual oil was distilled in vacuo to give 17.5 g (95%) of a mixture of the (Z)- and (E)-isomer of 7c. The mixture (3.2 g) could be separated by column chromatography on silica gel (50 g). The CHCl₃ eluate gave 1.80 g of (E)-7c and 0.57 g of (Z)-7c.

Compounds 7a, b, d, e were obtained from 1a, b, d, e, respectively, in the same way. The results are shown in Table III.

Reaction D. (Z)-3-Phenyl-3-(2-pyridyl)acrylonitrile [Z]-7c — A mixture of 1.12 g (5 mmol) of (Z)-8c and 0.79 g (10 mmol) of pyridine in 30 ml of dioxane was treated with 1.16 g (5.5 mmol) of (CF₃CO)₂O at 10–15° with stirring. The mixture was stirred at room temperature for 2 hr and then concentrated in vacuo. The residue was mixed with 10% Na₂CO₃ solution and extracted with Et₂O. The extract was washed with H₂O, dried, and concentrated in vacuo. The residue was purified by silica gel (10 g) chromatography to give 0.67 g (68%) of [Z]-7c.
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<th>(Z)-Isomer Yield (%)</th>
<th>mp (Solvent) IR (cm⁻¹)</th>
<th>Analysis (%)</th>
<th>(E)-Isomer Yield (%)</th>
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a) Yield of a mixture of the (Z)- and (E)-isomers.
b) Determined by NMR spectroscopy or NPLC.

c) Yield of separated (Z)- and (E)-isomer, as indicated.

d) Formula (Call): 6c = C₆H₅NO₂ (C, 75.87; H, 6.92; N, 6.85; 6d = C₆H₅NO₂ (C, 75.87; H, 6.92; N, 6.85; 6e = C₆H₅NO₂ (C, 75.87; H, 6.92; N, 6.85; 6f = C₆H₅NO₂ (C, 75.87; H, 6.92; N, 6.85).

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a) Formula (Caled): 12e—e=C₆H₅NO₂; C (75.25; H, 6.71; N, 5.89); 13e—e=C₆H₅NO₂; C (76.65; H, 8.57; N, 11.50), 14e—e=C₆H₅NO₂; C (76.43; H, 6.81; N, 16.49).  
b) Solvent: CDCl₃.  
c) Boiling and melting points reported in the literature are as follows: 12a—bp 118° (0 mmHg), 12b—bp 190-195° (1 mmHg); 12c—bp not described; 12d—mp 29-30°, 13a—mp not described, 13b—mp 88-90°, 14a—mp 92.5-94.5° (maleate), 14b—mp 101°, 14c—mp 122-123°.

Other experimental results are shown in Table III.

**Reaction E. 3-Phenyl-3-(4-pyridyl)acrylamide (8e)** — An ice-cold solution of 2.30 g (0.11 mmol) of Na metal in 75 ml of EtOH was treated with 20 g (0.11 mmol) of 4 and stirred at 5-10° for 10 min. Next, 16.5 g (0.09 mol) of 1e was added. After stirring at room temperature for 1 hr, the mixture was heated at 50-60° for 1 hr and concentrated in vacuo. The resulting crystalline material was filtered and washed with H₂O to give 16.8 g (83%) of crude 8e as a mixture of the (Z)- and (E)-isomers. The mixture could be separated by column chromatography on silica gel (400 g). Elution with MeOH-CHCl₃ (1:100) gave 11.5 g (58%) of (Z)-8e and 4.4 g (22%) of (E)-8e.

Compounds 8a—d were obtained from 1a—d, respectively, in the same way. The mixtures of (Z)- and (E)-isomers of 8c, d could also be separated by column chromatography on silica gel. The results are shown in Table III.

**Reaction F. (E)-3-Phenyl-3-(2-pyridyl)acrylamide [(E)-8c]** — A mixture of 0.50 g (2.4 mmol) of (E)-7c and 1.5 g of conc. H₂SO₄ in 1.5 g of AcOH was heated at 100° for 4 hr then poured into ice-water. The mixture was made basic with 10% Na₂CO₃ solution and insoluble material was collected to give 0.38 g (70%) of (E)-8c.

Other experimental results are shown in Table III.

**Reaction G. Ethyl N-isopropyl-3-phenyl-2-butenonimidate (9a)** — A mixture of 4.85 g (30 mmol) of FeCl₃ in 20 ml of 2-chloropropane was treated with 4.30 g (30 mmol) of 7a at 0° with stirring. The mixture was refluxed with stirring for 4 hr and cooled to 0° in an ice-bath. Next, 4.5 ml of EtOH was added below 5° with stirring, and the mixture was poured into 100 ml of 10% Na₂CO₃ solution. The organic layer was separated and the water layer was extracted with Et₂O. The combined organic layer was washed with H₂O, dried and concentrated in vacuo. The residue was distilled in vacuo to give 6.7 g (87%) of 9a, bp 182-184° (9 mmHg). IR ν max cm⁻¹: 2960, 1665. NMR δ (CDCl₃): 7.5 (5H, m, C₆H₅), 6.30 (1H, s, =CH), 4.25 (2H, q, O-CH₂), 3.72 (1H, m, N-CH), 2.20 (3H, s, CH₃), 1.33 (3H, t, CH₃), 1.10 (6H, d, CH₂). Anal. Calcd for C₁₃H₁₆N-O: C, 77.88; H, 9.15; N, 6.06. Found: C, 77.84; H, 9.05; N, 6.01.

Following a procedure similar to that used for the synthesis of 9a, 2.05 g (10 mmol) of 7b was treated with 1.60 g FeCl₃ in 20 ml of 2-chloropropane and then with 1.5 ml of EtOH to give 2.6 g (89%) of 9b, bp 113-115° (2 mmHg). IR ν max cm⁻¹: 2960, 1660. NMR δ (CDCl₃): 7.5 (5H, m, C₆H₅), 7.3-8.0 (5H, m, C₆H₅), 6.41 (1H, s, =CH), 3.95 (2H, q, O-CH₂), 3.72 (1H, m, N-CH), 0.96 (6H, d, CH₂), 0.90 (3H, t, CH₃). Anal. Calcd for C₁₃H₁₆N-O: C, 81.87; H, 7.90; N, 4.77. Found: C, 81.50; H, 7.98; N, 4.77.

**Reaction H. 2-(2-phenyl-1-propenyl)-2-imidazoline (11a)** — A mixture of 2.31 g (10 mmol) of 9a and 0.90 g (15 mmol) of ethylidenemaine was heated at 110-120° for 1 hr. After cooling, the reaction mixture was dissolved in Et₂O and the solution was washed with satd. NaCl solution, dried, and concentrated to give 0.56 g (32%) of 11a.

Compound 11b was obtained in a similar way. The results are shown in Table III.

**Reaction I. (E)-Ethyl 3-Phenyl-3-(2-pyridyl)acrylamide [(E)-10c]** — The hydrochloride of (E)-8c (2.60 g, 10 mmol) was added to a solution of Meerwein salt, prepared from 5.80 g (40 mmol) of BF₄⁻Et₂O and 2.90 g (40 mmol) of epichlorohydrin, in 40 ml of CH₂Cl₂. The mixture was heated under reflux with stirring overnight and then poured into cold satd. NaHCO₃ solution. The organic layer was separated and the water layer was extracted with CHCl₃. The combined organic layer was washed with H₂O, dried, and concentrated in vacuo. The residue was mixed with a large amount of petr. ether and insoluble material was filtered off. The filtrate was concentrated in vacuo to give 1.55 g (62%) of (E)-10c as a crude oil which was used for the subsequent reaction without further purification.

Other experimental results are shown in Table III.

**Reaction J. (E)-2-(2-phenyl-2-(2-pyridyl)ethenyl)-2-imidazoline [(E)-11c]** — A solution of 1.55 g (6.2 mmol) of crude (E)-8c and 0.73 g (12 mmol) of ethylidenemaine in 15 ml of EtOH was refluxed for 2 hr.
The mixture was concentrated in vacuo and the residue was dissolved in Et₂O. The solution was washed with satd. NaCl solution, dried, and concentrated in vacuo to give 1.08 g (70%) of (E)-11c.

Compounds 11b, d, e were similarly obtained from 8b, d, e, respectively, by the method described above. The results are shown in Table III.

**Reaction K.** 2-(2-Phenyl)-2-(2-pyridyl)ethenyl-2-imidazoline (11c)—An ice-cold solution of 0.46 g (20 mmol) of Na metal in 15 ml of EtOH was treated with 4.44 g (20 mmol) of 3 and stirred at 5—10° for 10 min. Next, 2.78 g (15 mmol) of 1c was added. The mixture was stirred at room temperature for 8—10 hr then concentrated in vacuo. The residue was mixed with H₂O and neutralized to pH 6—7 adding conc. HCl. After washing the mixture with Et₂O to remove the unchanged ketone (1c), the mixture was made basic with conc. NaOH solution and extracted with CHCl₃. The extract was washed with satd. NaCl solution, dried, and concentrated in vacuo to give 2.52 g (70%) of oily 11c as a mixture of the (Z)- and (E)-isomers. Compounds 11a, b, d, e were similarly obtained from 1a, b, d, e, respectively, in the manner described above, except in the cases of 1a, b, which were refluxed for 10—20 hr. The results are shown in Table III.

**Reaction L.** Ethyl 3-phenyl-3-(4-pyridyl)propionate (12c)—Compound 6e (4.60 g, 16 mmol) in 20 ml of EtOH was hydrogenated over 2.5 g of 5% Pd-C catalyst at room temperature under atmospheric pressure. When H₂ absorption ceased, the catalyst was filtered off and the filtrate was concentrated in vacuo. The residue was distilled in vacuo to give 3.70 g (93%) of 12c.

Compounds 12a—d, 13a, b were obtained similarly from 6a—d, 7a, b, respectively, in the manner described above. The results are shown in Table IV.

**Reaction M.** 3-Phenyl-3-(2-pyridyl)propionitrile (13c)—A mixture of 2.06 g (10 mmol) of 7c and 2.00 g of NaBH₄ in 50 ml of EtOH was refluxed for 8 hr then concentrated in vacuo. The residue was mixed with H₂O and extracted with Et₂O. The extract was washed with H₂O, dried, and concentrated in vacuo. The remaining oil was distilled in vacuo to give 1.36 g (65%) of 13c, bp 166—169° (2 mmHg).

Compounds 13d, e were obtained from 7d, e, respectively, in the manner described above. The results are shown in Table IV.

**Reaction N.** 2-(2-Phenylpropyl)-2-imidazoline (14a)⁶—A mixture of 13.4 g (70 mmol) of 12a and 42.0 g (0.7 mol) of ethylenediamine was refluxed for 20 hr. Excess ethylenediamine was evaporated off at atmospheric pressure. Next, 1.50 g of Mg metal was added and the mixture was heated at 230—240° for 2 hr under an N₂ atmosphere. The reaction residue was distilled in vacuo to give 9.40 g (72%) of 14a.

Compounds 14b—e were obtained from 12b—e, respectively, in a similar manner. The results are shown in Table IV.

**Reaction O.** 2-(2,2-Diphenylethyl)-2-imidazoline (14b)—A mixture of 2.07 g (10 mmol) of 13b and 2.78 g (12 mmol) of ethylenediamine monosolesylate was heated at 200—220° for 3 hr. After cooling, the residue was treated with 10% NaOH solution and extracted with CHCl₃. The extract was washed with H₂O, dried, and concentrated in vacuo to give 1.40 g (56%) of 14b.

Compounds 14c—e were similarly prepared from 13c—e, respectively. The results are shown in Table IV.

**Reaction P.** 2-(2,2-Diphenylethyl)-2-imidazoline (14b)—Compound 11b (3.70 g, 13 mmol) in 10 ml of EtOH was hydrogenated over 0.30 g of 5% Pd-C and worked up in the usual way to give 2.70 g (83%) of 14b.

Compounds 14a, c—e were obtained from 11a, c—e, respectively, in a similar manner. The results are shown in Table IV.

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