2-Imidazolines. III (1). 1-Aryl- and 1-acyl-2-amino-(or methoxy)-4,5-diamino-4,5-dihydroimidazoles. Synthesis and Properties

*Luisa Citerio, Elisabetta Rivera, Maria Luisa Saccarello, Riccardo Stradi**

Istituto di Chimica Organica della Facoltà di Farmacia, Università di Milano, Viale Abruzzi 42, 20131 Milano, Italy

Bruno Gioia

Farmitalia-C.Erba S.p.A., Ricerca e Sviluppo chimico, Via Dei Gracchi 35, 20146 Milano, Italy

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Diimmonium salt (**5**) reacts with guanidines (**6**) and *o*-methylisoureas (**7**) affording 2-amino-4,5-dimorpholinoimidazolines (**9**). 1-Aryl-2-amino-4,5-dimorpholinoimidazolines lose the amino functionality under mild acidic conditions with formation of 2-amino-5-morpholinoimidazole derivatives (**10**) whereas 1-acyl derivatives undergo under the same conditions a ring expansion process leading to pyrimidine derivatives (**13**).

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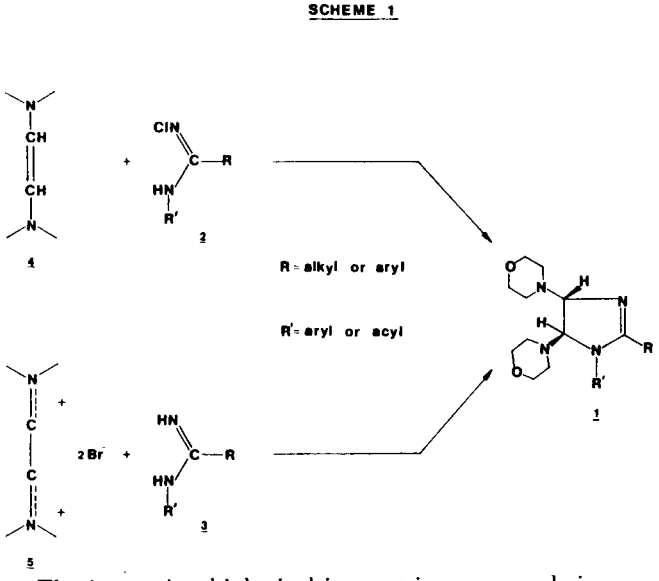
Recently, we reported the preparation of 1-aryl- and 1-acyl-2-aryl(or alkyl)-4,5-diamino-4,5-dihydroimidazoles (**1**) by reaction of *N*-chloroamidines (**2**) with 1,2-diaminoethenes (**4**) (2,3) or, more practicably, from amidines (**3**) and the diimmonium dibromide (**5**) (4).

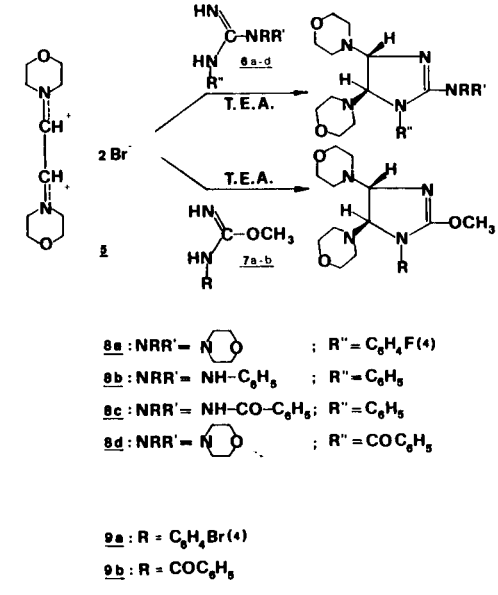
SCHEME 1



The increasing biological interest in compounds incorporating the imidazole ring prompted us to extend this reaction to the synthesis of 2-amino and 2-alkoxy substituted derivatives. In this paper we wish to report our findings from this study.

The diimmonium dibromide (**5**) reacts under mild conditions with guanidines (**6a-d**) and with *o*-methylisoureas (**7a,b**) affording 2-amino-4,5-dimorpholinoimidazolines (**8a-d**) and 2-methoxy-4,5-dimorpholinoimidazolines (**9a,b**), respectively. In this case the above synthetic pathway proved to be by far the best because of the difficulties encountered in the purification of *N*-chloroguanidines and *N*-chloroisoureas which are the intermediates employed in the alternative method. Only three imidazolines (**8c, 8d** and **9b**) were prepared with both methods.

SCHEME 2



In all cases only the *trans* imidazoline was formed as confirmed by the values of the H_4-H_5 coupling constant ranging between 0 and 3 Hz.

The fragmentation pattern upon electron impact strongly depends on the nature of the substituents at N_1 and C_2. The main ions with their relative abundance are reported in the experimental.

Although the formation of two regioisomeric imidazolines would be foreseen from the reaction involving *N*-benzoyl-*N'*-phenylguanidine (**6c**), the sole product isolated was 2-benzoylamino-1-phenylimidazoline (**8c**).

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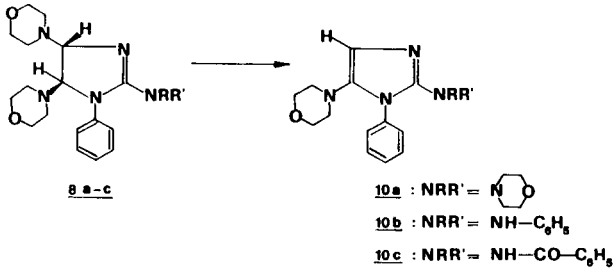
Clearly, the marked difference between the nucleophilicity of the nitrogen atoms present in **6c** regiospecifically controls the attack of **5** to form the isomer in which N_1 and N_3 were originally the more nucleophilic nitrogens of the guanidine.

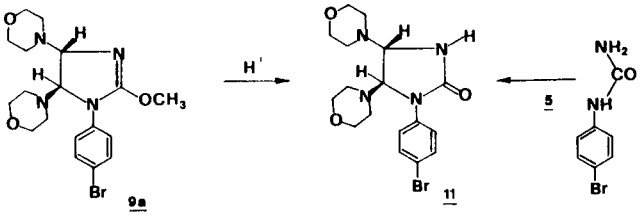
1-Phenyl-2-aminoimidazolines **8a-c** lose, under mild conditions, the amino group in position 4 affording, with almost quantitative yields, the corresponding 5-morpholinoimidazoles (**10a-c**). Confirmation of the 5-morpholinoimidazole structure for the deamination products was achieved by nmr and mass spectroscopic data as well as suggested by the parallel behaviour of 1,2-diaryl-4,5-dimorpholinoimidazoline (2).

SCHEME 3



Quite surprisingly, 1-(4-bromophenyl)-2-methoxyimidazoline **9a** afforded, under the same deamination conditions, 1-(4-bromophenyl)-4,5-dimorpholino-2-imidazolidinone **11** whose structure was confirmed by analytical and spectral data and by its independent preparation from the reaction between 4-bromophenylurea and the diimmonium salt **5**.

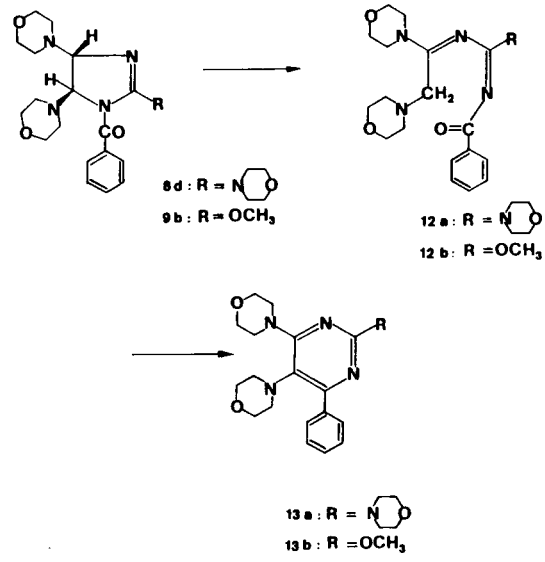
SCHEME 4



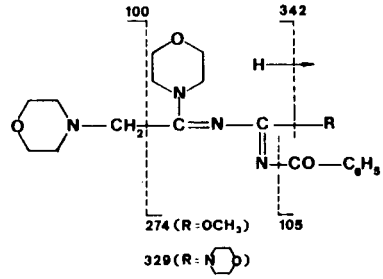
1-Aroyl derivatives **8d** and **9b** under the deamination conditions employed for **8a-c**, undergo a ring expansion process leading to pyrimidine derivatives (**13a** and **13b**). This reaction proceeds through an open chain intermediate which could be isolated carrying out the reaction at lower temperature or without the acidic catalysis.

The structure of *N*-(1,2-dimorpholinoethylidene)-*N'*-benzoylmorpholinoformamidine (**12a**) and *N*-(1,2-dimorpholinoethylidene)-*N'*-benzoylmethoxyformamidine (**12b**) respectively, was assigned on the basis of analytical, ^{1}H nmr and ir data and was confirmed by the mass spectra.

SCHEME 5



SCHEME 6



The behaviour of compounds **8d** and **9a** parallels that of 1-acylimidazolines without functionalization at C_2 (1) and thus confirms that the conversion of 1-acyl-4,5-diaminoimidazolines to pyrimidine derivatives is a general process independent of the nature of the substituent at C_2.

EXPERIMENTAL

Melting points were determined using a Büchi capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on Beckman Acculab 4 spectrometer using sodium chloride plates. Nmr spectra were recorded at 60 MHz using a Varian 360-A spectrometer. The chemical shift values are expressed as δ values relative to a tetramethyl silane internal standard. Mass spectra were recorded with a Varian MAT 311-A mass spectrometer at an electron energy of 70 eV. The direct insertion technique was used with a probe temperature of 70-100°. Column chromatography was performed using Merck silica gel (60-120 mesh) and thin layer chromatography was run on silica gel GF 254 plates.

Preparation of the Diimonium Salt (5).

The salt was prepared by the method described in reference (4) in a 10-40 mmoles scale and used immediately after preparation.

N-Benzoyl-*N'*-chloro-*N''*-phenylguanidine (**2b**).

To a solution of *N*-benzoyl-*N'*-phenylguanidine (**6c**) (5) (2.39 g., 10 mmoles) in dry dichloromethane (25 ml.), cooled at 0°, a solution of *t*-butyl hypochlorite (1.08 g., 10 mmoles) in dichloromethane (10 ml.) was added. After stirring at room temperature for 15 minutes the reaction mixture was washed with distilled water, the organic layer was dried over sodium sulfate and freed from the solvent under reduced pressure. The crude residue after crystallization from isopropyl ether gave 2.4 g. (91.2%) of **2b**, m.p. 88°; ir (nujol): 3210 and 3400 cm^{-1} (NH); 1690 cm^{-1} (C=O).

Anal. Calcd. for $C_{14}H_{12}ClN_3O$: C, 61.42; H, 4.41; N, 15.35. Found: C, 61.32; H, 4.52; N, 15.53.

N-Benzoyl-*N'*-chloromorpholinoformamidine (**2a**).

To a solution of *N*-benzoylmorpholinoformamidine (**6a**) (6) (2.33 g., 10 mmoles) in dry dichloromethane (25 ml.), cooled at 0°C, *t*-butyl hypochlorite (1.08 g., 10 mmoles in 10 ml. of dichloromethane) was added dropwise.

After stirring at room temperature for 15 minutes and usual working up 2.6 g. (98%) of **2a** was obtained, m.p. 119°; ir (nujol): 3240 cm^{-1} (NH), 1660 (C=O); nmr (deuteriochloroform): 3.42 (m, 4H, CH_2-N-CH_2), 3.8 (m, 4H, CH_2-O-CH_2), 7.4-7.75 and 7.8-8.1 (2m, 5H, aromatic), 8.3 (NH, exchangeable).

Anal. Calcd. for $C_{12}H_{14}ClN_3O_2$: C, 53.83; H, 5.27; N, 15.69. Found: C, 53.60; H, 5.31; N, 15.51.

N-benzoyl-*N'*-chloromethoxyformamidine (**2c**).

To a solution of *N*-benzoylmethoxyformamidine (**7b**) (7) (1.78 g., 10 mmoles) in dry dichloromethane (20 ml.) cooled at 0°C, a solution of *t*-butyl hypochlorite (1.08 g., 10 mmoles) in dichloromethane (10 ml.) was added dropwise. After stirring at room temperature for 30 minutes and the usual working up gave a crude residue which crystallized from cyclohexane yielded 2.07 g. (97.6%) of **2c**, m.p. 59° (8); ir (nujol): 3260 and 3400 cm^{-1} (NH), 1700 cm^{-1} (C=O).

Anal. Calcd. for $C_9H_9ClN_2O_2$: C, 50.83; H, 4.26; N, 13.17. Found: C, 50.87; H, 4.50; N, 13.19.

1-(4-Fluorophenyl)-2,4,5-trimorpholino-4,5-dihydroimidazole (**8a**).

To a well stirred suspension of diimonium salt **5** (3.58 g., 10 mmoles) in dry dichloromethane (50 ml.), cooled at −10°, a solution of *N*-(4-fluorophenyl)morpholinoformamidine (9) (6.69 g., 30 mmoles) dissolved in 70 ml. of dichloromethane was added dropwise. After stirring at room temperature for 30 minutes, the reaction mixture was filtered, the filtrate washed twice with water, the organic layer separated and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was crystallized from isopropyl ether yielding 3.32 g. (79%) of a white product melting at 144-146°; nmr (deuteriochloroform): 2.7 (m, 8H, CH_2-N-CH_2 at C_4), 3.33 (m, 4H, CH_2-N-CH_2 at C_2), 3.5-4.1 (m, 12H, CH_2-O-CH_2), 4.3 and 4.43 (2d, J = 1.5 Hz, H_4 and H_5), 6.9-7.7 (m, 4H, aromatic); ms: 419 (1, M^+), 332 (100), 275 (24), 217 (16), 211 (87), 181 (44), 125 (55), 122 (24), 99 (20), 95 (66), 77 (37), 76 (47).

Anal. Calcd. for $C_{21}H_{30}FN_5O_3$: C, 60.12; H, 7.20; N, 16.69. Found: C, 60.41; H, 7.44; N, 16.39.

4,5-Dimorpholino-1-phenyl-2-phenylamino-4,5-dihydroimidazole (**8b**).

A solution of *N,N'*-diphenylguanidine (**6b**) (2.11 g., 10 mmoles) in dry dichloromethane (50 ml.) containing 2.02 g. (20 mmoles) of triethylamine was added to a suspension of 3.58 g. of **5** as described in the above preparation. After analogous working up, a white-cream product was obtained which repeatedly crystallized from isopropyl ether yielded 2.97 g. (73%) of **8b** melting at 148°; nmr (deuteriochloroform): 2.58 (m, 8H, CH_2-N-CH_2), 3.68 (m, 8H, CH_2-O-CH_2), 4.25 and 4.7 (2d, J ≅ 0 Hz, 2H, H_4 and H_5), 4.83 (NH, exchangeable), 6.85-7.6 and 7.75-8.0 (2m, 10H, aromatic); ms: 407 (1, M^+), 320 (22), 262 (5), 87 (52), 86 (30), 77 (37), 57 (100), 56 (57).

Anal. Calcd. for $C_{23}H_{29}N_5O_2$: C, 67.78; H, 7.17; N, 17.18. Found: C, 67.53; H, 7.04; N, 16.88.

2-Benzoylamino-4,5-dimorpholino-1-phenyl-4,5-dihydroimidazole (**8c**).

Method A.

To a solution of *N*-benzoyl-*N'*-phenyl-*N''*-chloroguanidine (**2b**) (2.73 g., 10 mmoles) and pyridine (0.79 g., 10 mmoles) in 30 ml. of dry dichloromethane, 1.98 g. (10 mmoles) of 1,2-dimorpholinoethylene (11) dissolved in dry dichloromethane (30 ml.) were added. After stirring at room temperature for 90 minutes, the reaction mixture was washed with a sodium bicarbonate solution. The organic layer, dried over sodium sulfate, was evaporated under reduced pressure and the crude residue chromatographed on a silica gel column [silica/crude product (40:1), eluent: benzene/ethyl acetate (80:20). The main fraction, after evaporation of the solvent, afforded 1.06 g. (24.5 %) of **8c** which recrystallized from ethyl ether, melts at 176-179° dec.; ir (nujol): 3300 cm^{-1} (NH), 1600 cm^{-1} (C=O); nmr (deuteriochloroform): 2.64 (m, 8H, CH_2-N-CH_2), 3.76 (m, 8H, CH_2-O-CH_2), 4.53 and 4.83 (2d, J = 0.5 Hz, 2H, H_4 and H_5), 7.2-7.9 and 8.0-8.35 (2m, 10H, aromatic), 9.83 (NH, exchangeable); ms: 435 (4, M^+), 348 (60), 330 (5), 243 (100), 191 (67), 140 (22), 105 (80), 77 (74).

Anal. Calcd. for $C_{24}H_{29}N_5O_3$: C, 66.18; H, 6.71; N, 16.08. Found: C, 65.86; H, 6.83; N, 15.82.

Method B.

A solution of *N*-benzoyl-*N'*-phenylguanidine (**6c**) (2.39 g., 10 mmoles) and triethylamine (2.02 g., 20 mmoles) in 50 ml. of dry dichloromethane was added to a suspension of 3.58 g. of **5** in the same manner as described for **8a**. After the usual working up 2.52 g. (58%) of **8c** melting at 178-179° were obtained.

1-Benzoyl-2,4,5-trimorpholino-4,5-dihydroimidazole (**8d**).

Method A.

To a solution of *N*-benzoyl-*N'*-chloromorpholinoformamidine (**2a**) (2.67 g., 10 mmoles) and pyridine (0.79 g., 10 mmoles) in dry dichloromethane (30 ml.), 1.98 g. (10 mmoles) of 1,2-dimorpholinoethylene dissolved in 30 ml. of dichloromethane were added. After stirring at room temperature for 15 minutes, the reaction mixture was washed with a solution of sodium bicarbonate, dried over sodium sulfate, and the solvent evaporated under reduced pressure. The crude residue was crystallized from ethanol affording 4.1 g. (95%) of **8d**; m.p. 175°; ir (nujol): 1645 cm^{-1} (C=O); nmr (deuteriochloroform): 2.64, 3.26, 3.76 (3m, 24H, morpholine protons), 4.22 and 4.86 (2d, J = 1.0 Hz, 2H, H_4 and H_5), 7.35-8.0 (m, 5H, aromatic); ms: 429 (1, M^+), 324 (100), 237 (17), 211 (20), 181 (18), 125 (15), 105 (34), 100 (19), 77 (28).

Anal. Calcd. for $C_{22}H_{31}N_5O_4$: C, 61.51; H, 7.27; N, 16.30. Found: C, 61.17; H, 7.33; N, 16.06.

Method B.

A solution of *N*-benzoylmorpholinoformamidine (**6a**) (2.33 g., 10 mmoles) and triethylamine (2.02 g., 20 mmoles) in 50 ml. of dry dichloromethane was added to a suspension of 3.58 g. of **5** in the same manner as described for **8a**. After the usual working up 4.15 g. (96.5%) of **8d** melting at 175° were obtained.

1-(4-Bromophenyl)-4,5-dimorpholino-2-methoxy-4,5-dihydroimidazole (**9a**).

A solution of *N*-(4-bromophenyl)methoxyformamidine (**7a**) (12) (2.29 g., 10 mmoles) and triethylamine (2.02 g., 20 mmoles) in dry dichloromethane (50 ml.) was added to a suspension of 3.58 g. of **5** in the same way as described for **8a**. After the usual working up, the crude residue was chromatographed on a silica gel column [silica/crude product (40:1), eluent: tetrahydrofuran]. The main fraction after evaporation of the solvent, afforded **9a** as a white crystalline product melting at 117-119° (from ethanol); nmr (deuteriochloroform): 2.63 (m, 8H, CH_2-N-CH_2), 3.73 (m, 8H, CH_2-O-CH_2), 4.0 (s, 3H, -OCH_3), 4.4 and 4.76 (2d, J = 2.6 Hz, 2H, H_4 and H_5), 7.1-7.7 (m, 4H, aromatic); ms: 426-424 (0.3, M^+), 411-409 (3), 199-197 (1), 141 (100).

Anal. Calcd. for $C_{18}H_{25}BrN_4O_3$: C, 50.82; H, 5.92; N, 13.17. Found: C, 50.56; H, 5.90; N, 13.47.

1-Benzoyl-4,5-dimorpholino-2-methoxy-4,5-dihydroimidazole (**9b**).

Method A.

To a solution of *N*-benzoyl-*N'*-chloromethoxyformamidine (**2c**) (2.12 g., 10 mmoles) and pyridine (0.79 g., 10 mmoles) in dry dichloromethane (30 ml.), 1.98 g. (10 mmoles) of 1,2-dimorpholinoethylene dissolved in dichloromethane (30 ml.) were added. After stirring at room temperature for 45 minutes and usual working up 3.25 g. (87%) of imidazoline (**9b**) were obtained, m.p. 176° (from 2-propanol); ir (nujol): 1660 cm^{-1} (C=O); nmr (deuteriochloroform): 2.66 (m, 8H, CH_2-N-CH_2), 3.65 (m, 11H, CH_2-O-CH_2, -OCH_3), 4.3 and 5.38 (2d, J = 2.2 Hz, 2H, H_4 and H_5), 7.2-7.7 (m, 5H, aromatic); ms: 374 (0.2 M^+), 269 (100), 141 (41), 105 (22), 77 (16).

Anal. Calcd. for $C_{19}H_{26}N_4O_4$: C, 60.94; H, 6.99; N, 14.96. Found: C, 60.58; H, 6.84; N, 14.68.

Method B.

A solution of *N*-benzoylmethoxyformamidine (**7b**) (1.78 g., 10 mmoles) and triethylamine (2.02 g., 20 mmoles) in 50 ml. of dry dichloromethane was added to a suspension of 3.58 g. of **5** in the usual way. After the usual working up, 3.4 g. (30%) of **9b**, m.p. 176° were obtained.

2,5-Dimorpholino-1-(4-fluorophenyl)imidazole (**10a**).

1-(4-Fluorophenyl)-2,4,5-trimorpholino-4,5-dihydroimiazole (**8a**) (4.19 g., 10 mmoles) was refluxed for 19 hours in dry chloroform (50 ml.) and in the presence of an equimolar amount of triethylamine hydrochloride (1.37 g.). The reaction mixture was cooled at room temperature, then washed with a sodium bicarbonate solution, dried over sodium sulfate and freed from the solvent under reduced pressure. The crude residue was purified through a silica gel column silica/crude product (40:1) eluent: tetrahydrofuran affording pure **10a** 3.2 g. (97%); m.p. 136° (from isopropyl ether); nmr (deuteriochloroform): 2.5-3.3 (m, 8H, CH_2-N-CH_2), 3.5-3.9 (m, 8H, CH_2-O-CH_2), 6.4 (s, 1H, H_4), 6.9-7.7 (m, 4H, aromatic); ms: 332 (100, M^+), 275 (18), 274 (10), 217 (15), 198 (10), 122 (14), 109 (15), 95 (21), 86 (13).

Anal. Calcd. for $C_{17}H_{21}FN_4O_2$: C, 61.42; H, 6.36; N, 16.85. Found: C, 61.31; H, 6.21; N, 16.93.

5-Morpholino-1-phenyl-2-phenylaminoimidazole (**10b**).

4,5-Dimorpholino-1-phenyl-2-phenylamino-4,5-dihydroimidazole (**8b**) (4.07 g., 10 mmoles) was chromatographed on a silica gel column containing 150 g. of silica eluting with benzene/tetrahydrofuran (70:30). During this operation, the deamination process occurs and the imidazole **10b** was collected as the main fraction (3 g., 94%), m.p. 166-167° (from 2-propanol); ir (nujol): 3480 cm^{-1} (NH); nmr (deuteriochloroform): 2.6 (m, 4H, CH_2-N-CH_2), 3.43 (m, 4H, CH_2-O-CH_2), 5.63 (NH, exchangeable); ms: 320 (21, M^+), 104 (9), 78 (100), 77 (45), 52 (23), 51 (32), 50 (25).

Anal. Calcd. for $C_{19}H_{20}N_4O$: C, 71.22; H, 6.29; N, 17.48. Found: C, 71.50; H, 6.50; N, 17.23.

2-Benzoylamino-5-morpholino-1-phenylimidazole (**10c**).

2-Benzoylamino-4,5-dimorpholino-1-phenyl-4,5-dihydroimidazole (**8c**) (4.35 g., 10 mmoles) was refluxed in dry xylene for 16 hours. After cooling, the white precipitate was filtered off and washed with dry benzene yielding 3.2 g. (92%) of (**10c**); m.p. 207-209°; ir (nujol): 3180 cm^{-1} (NH), 1610-1630 cm^{-1} (CO); nmr (deuteriochloroform): 2.63 (m, 4H, CH_2-N-CH_2), 3.5 (m, 4H, CH_2-O-CH_2), 6.2 (s, 1H, H_4), 6.8-7.7 and 7.8-8.3 (2m, 11H, aromatic and NH exchangeable); ms: 348 (61, M^+), 243 (100), 140 (10), 106 (35), 105 (43), 104 (17), 91 (66), 77 (56).

Anal. Calcd. for $C_{20}H_{20}N_4O_2$: C, 68.94; H, 5.78; N, 16.08. Found: C, 68.87; H, 5.69; N, 15.98.

1-(4-Bromophenyl)-4,5-dimorpholino-2-imidazolidinone (**11**).

A) From Imidazoline **9a**.

1-(4-Bromophenyl)-4,5-dimorpholino-2-methoxy-4,5-dihydroimidazole (**9a**) (4.25 g., 10 mmoles) was refluxed in 1,1,2-trichloroethane (50 ml.) in the presence of an equimolar amount of triethylamine hydrochloride for 5 hours. After the usual working up, 1.69 g. (41.3%) of a white product melting at 200° (from ethanol) were isolated; ir (nujol): 3280 cm^{-1} (NH), 1720-1700 (C=O), nmr (deuteriochloroform): 2.6 (m, 8H, CH_2-N-CH_2), 3.66 (m, 8H, CH_2-O-CH_2), 4.3 and 4.7 (2d, J = 1.0 Hz, 2H, H_4 and H_5), 6.7 (NH, exchangeable), 7.1-7.9 (m, 4H, aromatic); ms: 412-410 (4, M^+), 325 (20), 323 (14), 271 (13), 269 (14), 141 (25), 100 (100), 57 (24).

Anal. Calcd. for $C_{17}H_{23}BrN_4O_3$: C, 49.63; H, 5.63; N, 13.62. Found: C, 49.51; H, 5.39; N, 13.81.

B) From *N*-(4-Bromophenyl)urea.

A solution of *N*-(4-bromophenyl)urea (2.15 g., 10 mmoles) and triethylamine (2.02 g., 20 mmoles) in dry dichloromethane (50 ml.) was added to a suspension of 3.58 g. of **5** in the same way as described for **8a**. After the usual working up, the crude residue was chromatographed on a silica gel column (silica/crude product) (40:1), eluent: tetrahydrofuran/benzene (50:50) yielding a crystalline product melting at 197-200° (from ethanol). This compound proved to be identical (ir, nmr, ms) to imidazolidinone (**11**).

6-Phenyl-2,4,5-trimorpholinopyrimidine (**13a**) and *N*-Benzoyl-*N'*-(1,2-dimorpholino)ethylidenemorpholinoformamidine (**12a**).

1-Benzoyl-2,4,5-trimorpholino-4,5-dihydroimidazole (**8d**) (4.29 g., 10 mmoles) was refluxed with triethylamine hydrochloride (1.375 g., 10 mmoles) in dry xylene (50 ml.) for 24 hours.

The reaction mixture, washed with water, was dried with sodium sulfate and evaporated under reduced pressure. The crude residue was crystallized from isopropyl ether/ethanol (50:50) affording 3.65 g. (89%) of **13a**; m.p. 169° dec.; nmr (deuteriochloroform): 2.7 (m, 4H, CH_2-N-CH_2 at 5 pos.), 3.4-4.1 [m, 20H, CH_2-O-CH_2, $(CH_2)_2$=N-C=N], 7.52 (s, 5H, aromatic); ms: 411 (100, M^+), 380 (35), 366 (18), 352 (21), 322 (27), 308 (18), 296 (15), 264 (15), 237 (16), 128 (22).

Anal. Calcd. for $C_{22}H_{29}N_5O_3$: C, 64.21; H, 7.10; N, 17.02. Found: C, 63.90; H, 7.00; N, 16.9.

When dihydroimidazole (**8d**) (4.29 g., 10 mmoles) was refluxed with triethylamine hydrochloride (1.375 g., 10 mmoles) in dry toluene (150 ml.) for 3 hours, *N*-benzoyl-*N'*-(1,2-dimorpholino)ethylidenemorpholinoformamidine (**12a**) 3.95 g. (92%) was isolated, m.p. (isopropyl ether) 142-144° dec.; nmr (deuteriochloroform): 2.36 [m, 4H, $(CH_2)_2$=N-CH_2], 3.25 (s, 2H, -CH_2-), 3.5-4.0 [m, 20H, CH_2-O-CH_2 and $(CH_2)_2$=N-C=], 7.3-7.7 and 8.0-8.4 (2m, 5H, aromatic); ms: 429 (12, M^+), 342 (14), 329 (5), 261 (6), 258 (8), 237 (28), 114 (24), 105 (100), 100 (25), 77 (53).

Anal. Calcd. for $C_{22}H_{31}N_5O_4$: C, 61.51; H, 7.27; N, 16.30. Found: C, 61.41; H, 7.40; N, 16.23.

4,5-Dimorpholino-2-methoxy-6-phenylpyrimidine (**13b**) and *N*-benzoyl-*N'*-(1,2-dimorpholino)ethylidenemethoxyformamidine (**12b**).

1-Benzoyl-4,5-dimorpholino-2-methoxy-4,5-dihydroimidazole (**9b**) (3.74 g., 10 mmoles) and triethylamine hydrochloride (1.375 g., 10 mmoles) were refluxed for 24 hours in dry xylene (ml. 50). 3.1 g. (87%) of **13b** after the same working up described for **13a** were thus obtained, m.p. 171° dec. from isopropyl ether/ethanol (90:10); nmr (deuteriochloroform): 2.7 (t, 4H, CH_2-N-CH_2 at 5 pos.), 3.53 (t, 4H, CH_2-O-CH_2 at 5 pos.), 3.8 (s, 8H, morph. at 4 pos.), 4.9 (s, 3H, -OCH_3), 7.41 (s, 5H, aromatic); ms: 356 (100, M^+), 325 (87), 311 (30), 297 (23), 267 (34), 253 (37), 240 (57), 239 (64), 226 (35), 214 (33), 128 (45), 77 (75).

Anal. Calcd. for $C_{19}H_{24}N_4O_3$: C, 64.02; H, 6.78; N, 15.72. Found: C, 63.93; H, 6.55; N, 15.42.

When dihydroimidazole **9b** (3.74 g., 10 mmoles) was refluxed with triethylamine hydrochloride (1.375 g., 10 mmoles) in dry toluene (150 ml.) for 3 hours, *N*-benzoyl-*N'*-(1,2-dimorpholino)ethylidenemethoxyformamidine (**12b**) 3.47 g. (93%), was isolated in the same way as described for **12a**, m.p. 121-122° (from isopropyl ether); nmr (deuteriochloroform): 2.5 [m, 4H, $(CH_2)_2$=N-CH_2], 3.34 (s, 2H, -CH_2-C=), 3.65 [m, 12H, $(CH_2)_2$=N-C=, CH_2-O-CH_2], 4.01 (s, 3H, -OCH_3), 7.3-7.8 and 8.1-8.4 (2m, 5H, aromatic); ms: 374 (4, M^+), 342 (3), 289 (9), 287 (6), 274 (16), 237 (8), 121 (13), 114 (17), 105 (100), 100 (90), 77 (85).

Anal. Calcd. for $C_{19}H_{26}N_4O_4$: C, 60.94; H, 6.99; N, 14.96. Found: C, 61.00; H, 6.70; N, 14.75.

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