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Condensation of 2-methylimidazole with arylaldehyde **4** and subsequent reduction of the intermediate **5** with Raney-nickel gave 2-[2-(2,4-dichlorophenyl)ethyl]imidazole **2**. Compound **11** was prepared from compound **10** similarly. Reaction of compound **2** with methylsulfonyl chloride gave 1-methylsulfonyl-2-[2-(2,4-dichlorophenyl)ethyl]imidazole (**7a**) in moderate yield. Nitration of compound **11** (Ar = 3-pyridyl) gave the desired nitro compounds **14** and **15**.

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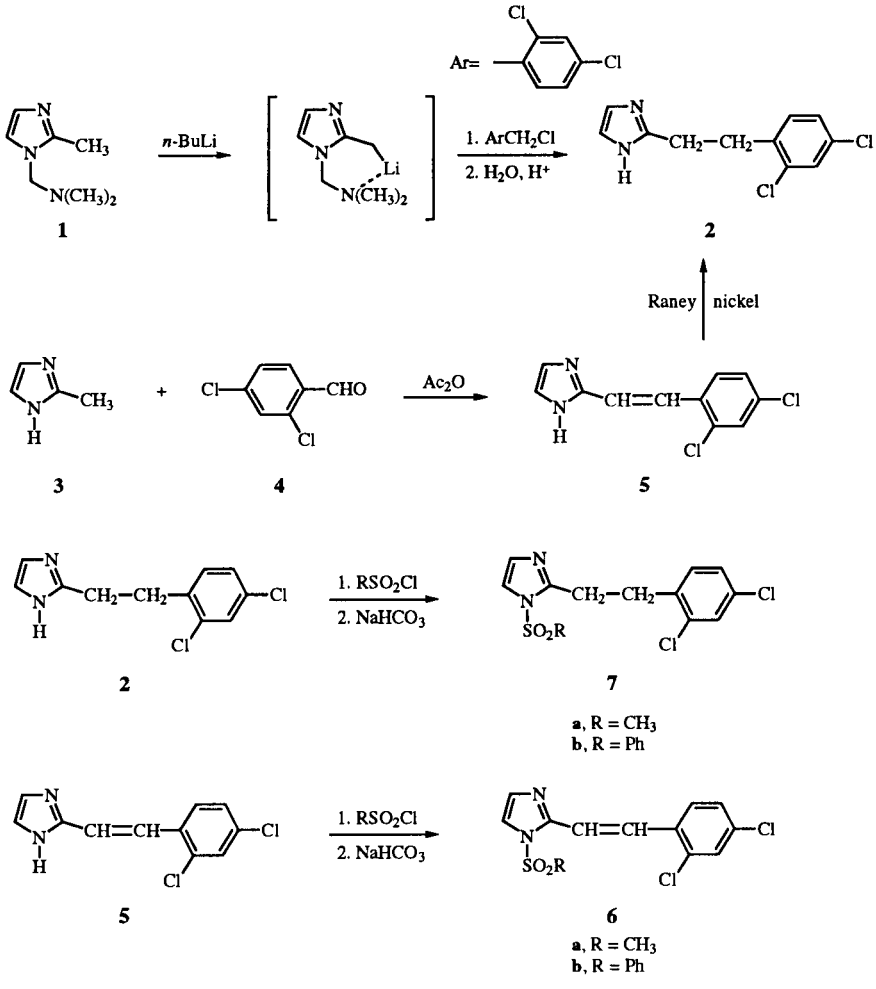
The considerable biological importance of imidazoles has stimulated much work on this heterocycle [1]. We would like to report the syntheses of the title compounds as possible effective drugs in fertility regulation [2].

The most common method for the preparation of 2-substituted imidazoles is alkylation of 1-(*N*,*N*-dimethylaminomethyl)-2-methylimidazole **1** in the presence of *n*-butyllithium to give 2-(2-arylethyl)imidazoles (Ar = 2,4-dichlorophenyl) **2** [3]. We could obtain compound **2** in moderate yield from the reaction of compounds **3** and **4** in the presence of acetic anhydride and subsequent reduction of the intermediate **5** with Raney-nickel [4,5]. Reaction of compound **5** with methylsulfonyl chloride (or benzenesulfonyl chloride) in the presence of sodium bicarbonate gave compounds **6a**, **6b**. Compounds **7a** and **7b** were prepared similarly [6] (Scheme 1).

Scheme 1



Direct alkylation of 1,2-dimethyl imidazole with 4-substituted benzyl halide gave compound **11** in low yield [7]. Reaction of 1,2-dimethyl imidazole with an aryl aldehyde in the presence of different alkoxide (such as methoxy, ethoxy and *tert*-butoxy) did not give the desired alcohols **9**. However compound **9** could be obtained by the reaction of compound **8** and an aldehyde in the presence of *n*-buthyllithium. Dehydration of compound **9** with acetic anhydride/acetic acid gave compound **10** [7].

Compound **10** (Ar = 3-pyridyl) could be also obtained from the reaction of compound **8** with 3-pyridine carboxyaldehyde in the presence of acetic anhydride. Reduction of compound **10** with Raney-nickel in dioxane afforded the desired compound **11** (Ar = 3-pyridyl) in excellent yield [4,5].

Nitration of compounds **11** (Ar = 3-pyridyl) with nitric acid-sulfuric acid at reflux temperature gave compounds **14** and **15**.

Scheme 2

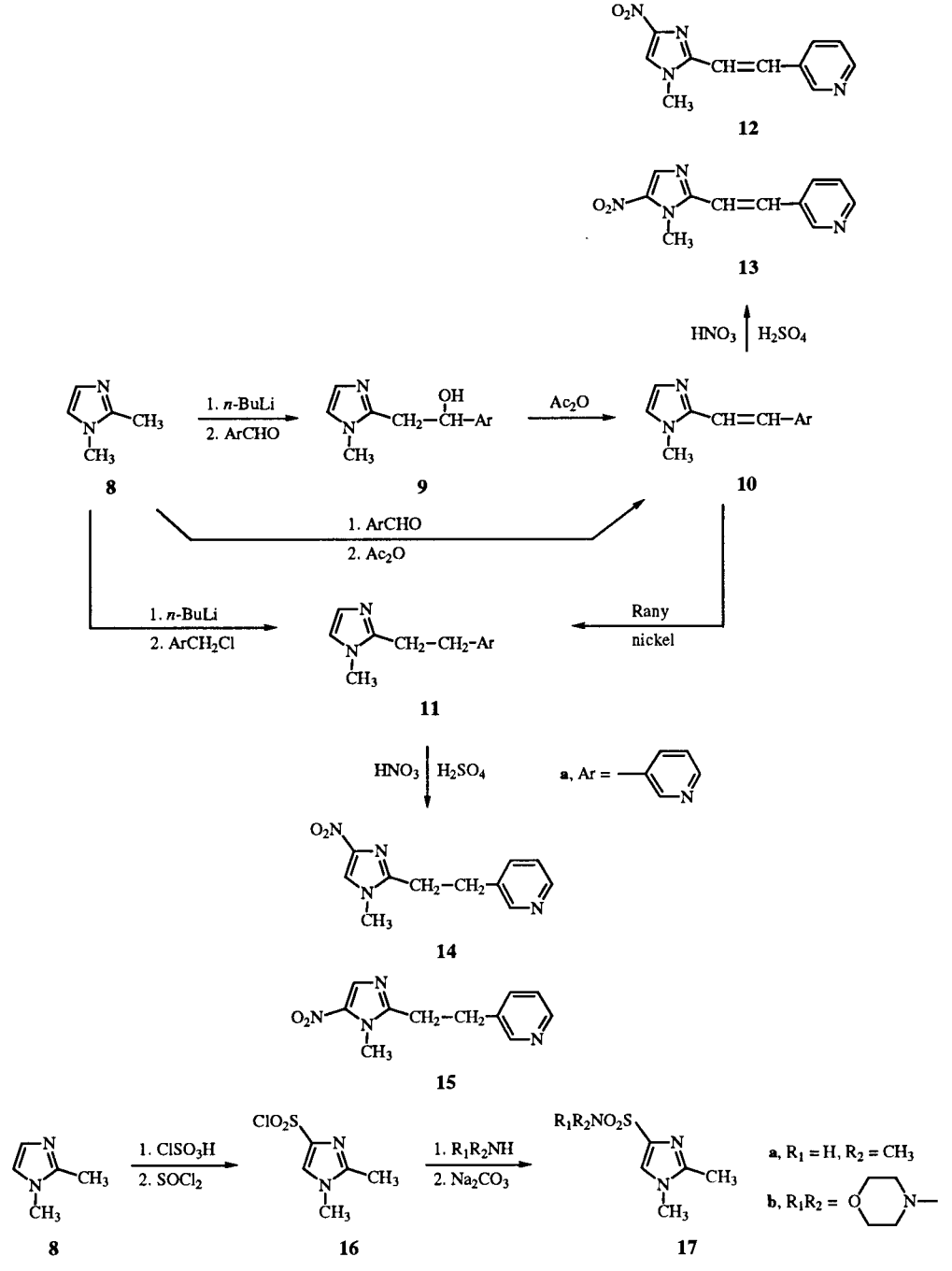


Table 1

| Compound | MP,°C | Yield % | Formula | Calcd. C% | Found C% | Calcd. H% | Found H% | Calcd. N% | Found N% |
|---|---|---|---|---|---|---|---|---|---|
| **6a** | 180-182 [a] | 89 | $C_{12}H_{10}Cl_2N_2O_2S$ | 45.42 | 45.24 | 3.15 | 2.99 | 8.83 | 8.90 |
| **6b** | 140 [a] | 75 | $C_{17}H_{12}Cl_2N_2O_2S$ | 53.82 | 53.62 | 3.16 | 2.98 | 7.38 | 7.45 |
| **7b** | Oil | 75 | $C_{17}H_{14}Cl_2N_2O_2S$ | 53.54 | 53.36 | 3.67 | 3.77 | 7.35 | 7.45 |
| **10a** | 114-115 [b] | 70 | $C_{11}H_{11}N_3$ | 71.35 | 71.25 | 5.94 | 6.11 | 22.70 | 22.89 |
| **11a** | Oil | 85 | $C_{11}H_{13}N_3$ | 70.59 | 70.41 | 6.94 | 6.80 | 22.46 | 22.85 |
| **12** | Oil | trace | $C_{11}H_{10}N_4O_2$ | 57.39 | 57.19 | 4.35 | 3.99 | 24.35 | 24.46 |
| **13** | Oil | 32 | $C_{11}H_{10}N_4O_2$ | 57.39 | 57.17 | 4.35 | 4.01 | 24.35 | 24.15 |
| **17a** | 223-225 [a] | 71 | $C_6H_{11}N_3O_2S$ | 38.09 | 37.90 | 5.82 | 6.96 | 22.22 | 22.15 |

[a] Compound **6** and **17a** were crystallized from ethanol. [b] Compound **10a**, was crystallized from chloroform-ether.

Assignment of structures of compounds **14** and **15** were made by spectroscopic data. It has been reported that in $^1$H-nmr spectrum, the δ value of 1-methyl in the 5-nitroimidazoles is greater than the 4-nitroimidazoles because of the greater deshielding effect of the 5-nitro group as compared with 4-position [8]. In compound **15** the 1-methyl group appeared 0.28 ppm lower field relative to the 1-methyl in compound **14**. This is in agreement with the suggested structures. Nitration of compound **10** (Ar = 3-pyridyl) similarly afforded compounds **12** and **13**.

Reaction of 1,2-dimethylimidazole **8** with chlorosulfonic acid and thionyl chloride gave 1,2-dimethyl-4-chlorosulfonylimidazole **16**. Reaction of compound **16** with an alkyl amine gave sulfonamides **17** [9].

The physical constants of the compounds prepared are summarized in Table 1.

## EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. The uv spectra were obtained using a Perkin-Elmer model 550 SE. The ir spectra were obtained using a Perkin-Elmer model 781 or Nicolet FT-IR Magna 550 spectrographs. The $^1$H-nmr spectra were obtained using Bruker FT-80 or Varian 400 Unity plus spectrometers and chemical shifts (δ) are in ppm relative to internal tetramethylsilane. Mass spectra were obtained using a Finnigan TSQ 70 Mass spectrophotometer at 70 ev.

2-[2-(2,4-Dichlorophenyl)ethenyl]imidazole (**5**).

A stirring mixture of 2,4-dichlorobenzaldehyde (8.75 g, 50 mmoles), 1,2-dimethylimidazole (4.1 g, 50 mmoles) and acetic anhydride (2.55 g, 25 mmoles) was heated at 140° for 3 hours. After cooling, water (50 ml) was added and acidified with hydrochloric acid. The mixture was extracted with ether. The aqueous layer was made alkaline with sodium bicarbonate and the precipitate was filtered and crystallized from ethanol to give 4.78 g (40%) of **5**; mp 200°; $^1$H nmr (deuteriochloroform): δ 7.89 (d, 1H, ethylene, J = 16 Hz), 7.38 (m, $H_3$ of phenyl), 7.23 (m, $H_5$, $H_6$ of phenyl) and 6.9 ppm (d, 1H, ethylene, J = 16 Hz); ms: m/z (%) 237 ($M^+$-1, 40), 203 (100), 162 (72), 83 (12), 43 (12).

*Anal.* Calcd. for $C_{11}H_8Cl_2N_2$: C, 55.23; H, 3.35; N, 11.71. Found: C, 55.01; H, 3.55; N, 11.65.

Compound **10** (Ar = 3-pyridyl) was prepared similarly (Table 1).

2-[2-(2,4-Dichlorophenyl)ethyl]imidazole (**2**).

A stirring mixture of compound **5** (2.4 g, 10 mmoles) in dioxane (20 ml) and Raney-nickel (8.8 g) was refluxed for 3 hours. After cooling, it was filtered. The solvent was evaporated and the residue was crystallized from chloroform to give 1.66 g (69%) of **2**; mp 135-137°; $^1$H nmr (deuteriochloroform): δ 7.66 (m, 6H, imidazole, phenyl and NH) and 3.77 ppm (s, 4H, $CH_2$-$CH_2$); ms: m/z (%) 241 ($M^+$+1, 90), 207 (93), 205 (100), 19 (15), 173 (77), 159 (57), 123 (24), 95 (81), 81 (95), 57 (15), 54 (27).

*Anal.* Calcd. for $C_{11}H_{10}Cl_2N_2$: C, 54.77; H, 4.15; N, 11.62. Found: C, 54.63; H, 4.30; N, 11.45.

Compound **11** was prepared similarly (Table 1).

1-Methylsulphonyl-2-[2-(2,4-dichlorophenyl)ethyl]imidazole (**7a**).

Compound **2** (0.24 g, 1 mmole) was added portionwise to a stirring solution of methylsulfonyl chloride (0.11 g, 1 mmole) in acetone (10 ml) in an ice bath and then a saturated solution of sodium bicarbonate (15 ml) was added to the mixture. After heating at 40° for 12 hours, the precipitate was filtered and washed with ice-water and the residue was crystallized from ethanol to give 0.14 g (89%) of **7a**, mp 117-118°; ir (potassium bromide): ν 3120 (C-H aromatic), 1370 ($SO_2$) and 1140 cm$^{-1}$ ($SO_2$); $^1$H-nmr (deuteriochloroform): δ 7.37 (s, 1H, $H_3$ of phenyl), 7.28 (d, 1H of imidazole, J = 1.6 Hz), 7.79 (m, $H_5$, $H_6$ of phenyl), 7.01 (d, 1H of imidazole, J = 1.6 Hz), 3.24 (s, 3H, $SO_2CH_3$) and 3.15 ppm (s, 4H, $CH_2$-$CH_2$), ms: m/z (%) 283 ($M^+$-Cl, 100), 205 (57), 203 (86), 159 (33), 95 (19), 81 (57), 79 (14).

*Anal.* Calcd. for $C_{12}H_{12}Cl_2N_2O_2S$: C, 44.86; H, 3.74; N, 8.72. Found: C, 45.02; H, 3.85; N, 8.60.

Compounds **6** and **7b** were prepared similarly (Table 1).

1-Methyl-2-[2-(3-pyridyl)ethyl]-4-nitroimidazole (**14**) and 1-Methyl-2-[2-(3-pyridyl)ethyl]-5-nitroimidazole (**15**).

Compound **11** (1.16 g, 5 mmoles) was added portionwise to a stirring mixture of nitric acid (9 ml, 65%) and concentrated sulfuric acid (9 ml) in an ice bath. The mixture was refluxed for 3 hours. After cooling to room temperature the mixture was added to ice-water. The precipitate was filtered, washed with ice-water to give a crude mixture of compounds **14** and **15** which were seperated by preparative tlc on silica gel using chloroform-ethanol (20:1) as the eluent. The fast moving fraction was crys-

tallized from ethanol to give 0.31 g (35%) of **15**, mp 135-138°; ir (potassium bromide): ν 3124 (C-H aromatic), 1520 ($NO_2$); and 1374 $cm^{-1}$ ($NO_2$), $^1$H-nmr (deuteriochloroform): δ 8.49 (m, $H_2$, $H_6$ of pyridine), 7.96 (s, 1H, $H_4$ of imidazole), 7.48 (m, $H_4$, $H_5$ of pyridine), 3.77 (s, 3H, $NCH_3$), and 3.09 (m, 4H, $CH_2CH_2$), ms: m/z (%) 233 ($M^+$, 100), 186 (43), 185 (36), 145 (21).

*Anal.* Calcd. for $C_{11}H_{12}N_4O_2$: C, 56.89; H, 5.17; N, 24.14. Found: C, 57.01; H, 5.35; N, 23.99.

The slow moving fraction was crystallized from ethanol to give 0.27 g (30%) of **14**, mp 133-136°; ir (potassium bromide): ν 3144 (C-H aromatic), 1538 ($NO_2$) and 1316 $cm^{-1}$ ($NO_2$), $^1$H-nmr (deuteriochloroform): δ 8.48 (m, $H_2$, $H_6$ of pyridine), 7.63 (s, 1H, $H_5$ of imidazole), 7.36 (m, $H_4$, $H_5$ of pyridine), 3.49 (s, 3H, $NCH_3$) and 3.07 ppm (m, 4H, $CH_2$-$CH_2$), ms: m/z (%) 233 ($M^+$, 100), 186 (57), 134 (15).

*Anal.* Calcd. for $C_{11}H_{12}N_4O_2$: C, 56.89; H, 5.17; N, 24.14. Found: C, 57.05; H, 5.32; N, 24.03.

Compounds **12** and **13** were prepared similarly (Table 1).

1,2-Dimethyl-4-chlorosulfonylimidazole (**16**).

1,2-Dimethylimidazole (9.6 g, 100 mmoles) was added portionwise to stirring chlorosulfonic acid (20 ml) in an ice bath. The mixture was heated gradually to 150°, stirred at this temperature for 6 hours and then cooled to room temperature. Thionyl chloride (11 ml) was added and the mixture was heated for 6 hours at 100°. After cooling to room temperature, the mixture was added to ice-water. The solution was neutralized with sodium carbonate. The resulting solid was filtered, washed with water and recrystallized from chloroform petroleum-ether to give 9.7 g (50%) of **16**, mp 90-91°; ir (potassium bromide): ν 3100 (C-H aromatic), 1370 ($SO_2$), 1270 (C-N) and 1110 $cm^{-1}$ ($SO_2$); $^1$H nmr (deuteriochloroform): δ 7.6 (s, 1H, $H_5$ of imidazole), 3.7 (s, 3H, $NCH_3$) and 2.45 ppm (s, 3H, $CH_3$), ms: m/z (%) 195 ($M^+$, 52), 159 (90), 130 (14), 95 (16), 56 (23), 43 (25), 42 (100).

*Anal.* Calcd. for $C_5H_7ClN_2O_2S$: C, 30.84; H, 3.60. Found: C, 30.70; H, 3.56.

1,2-Dimethyl-4-(4-morpholinolsulfonyl)imidazole (**17b**).

To a stirring solution of compound **16** (0.5 g, 3 mmoles) in dry acetonitrile was added dropwise a solution of morpholine (0.34 g, 3 mmoles) in dry acetonitrile (8 ml) . The mixture was stirred for 2 hours at room temperature. After evaporation of the acetonitrile *in vacuo* the residue was dissolved in water and neutralized with sodium carbonate. The mixture was let to stand in the refrigerator for 20 minutes. The resulting solid was filtered, washed with water and recrystallized from ethanol to give 0.6 g (82%) of **17b**, mp 213-215°; ir (potassium bromide): ν 3150 (C-H aromatic), 1328 ($SO_2$), 1255 (C-N) and 1170 $cm^{-1}$ ($SO_2$); $^1$H nmr (deuteriochloroform): δ 7.35 (s, 1H, $N_5$ of imidazole), 3.74 (m, 4H, $CH_2OCH_2$ of morpholine), 3.63 (s, 3H, $NCH_3$), 3.16 (m, 4H, $CH_2NCH_2$ of morpholine) and 2.3 ppm (s, 3H, $CH_3$); ms: m/z (%) 245 ($M^+$, 10), 23 (10), 190 (71), 172 (10), 160 (15), 96 (100), 56 (28).

*Anal.* Calcd. for $C_9H_{15}N_3O_3S$: C, 44.08; H, 6.12; N, 17.14. Found: C, 44.29; H, 6.35; N, 17.31.

Compound **17a** was prepared similarly (Table 1).

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