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CONVENIENT MODIFICATION OF THE LEIMGRUBER-BATCHO INDOLE SYNTHESIS: REDUCTION OF 2-NITRO-β-PYRROLIDINOSTYRENES BY THE $FeCl_3$–ACTIVATED CARBON–$N_2H_4 \cdot H_2O$ SYSTEM

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A new catalytic system containing ferric chloride, activated carbon, and hydrazine has been proposed for the reductive cyclization of β-dialkylamino-2-nitrostyrenes to give the corresponding indoles (Leimgruber-Batcho synthesis). Various substituted indoles may be obtained in high yield under these conditions.

Keywords: enamines, indoles, β-dialkylamino-2-nitrostyrenes, Leimgruber-Batcho synthesis, reductive cyclization.

The reduction of enamines obtained by the condensation of *o*-methylnitrobenzenes with DMF acetals, known as the Leimgruber-Batcho synthesis, is a commonly used method for the synthesis of indoles containing substituents at the ring positions 4–7 [1].

This condensation is most often carried out in DMF by heating the starting 2-methyl-1-nitrobenzene with the commercially available DMF dimethyl acetal. In the case of less active substrates, the N-pyrrolidinylformamide dimethyl acetal [2] or trialkylaminomethanes [3] may be useful but these reagents has to be specially prepared. The use of a mixture of the DMF dimethyl acetal with an equimolar amount of pyrrolidine has also been described [4]. This mixture acts similarly to the free N-pyrrolidinylformamide dimethyl acetal, which is apparently generated *in situ*.

The reduction of enamines is usually carried out by catalytic hydrogenation using molecular hydrogen in the presence of a palladium catalyst (Pd/C), hydrazine in the presence of palladium or sceletal nickel (Raney-Ni) catalyst, by the action of derivatives of Ti(III), Fe(II), Sn(II), and other reducing agents. Clark and Repke [5] have presented the most detailed review of these methods.

Unfortunately, all these methods have disadvantages. Catalytic hydrogenation requires special equipment and, furthermore, substituents in the substrate such as the OBn group or halogen atoms are rather

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often attacked. The nickel catalyst is rather soluble in the presence of atmospheric oxygen in the reaction mixture containing hydrazine and ammonia, and traces of nickel ions in the solution hinder the separation of indoles by causing the formation of tar.

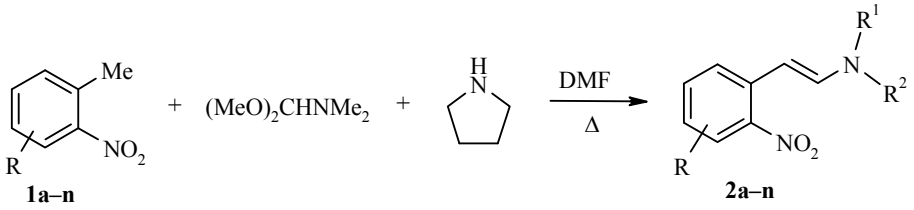
In our previous work [6], we reported that the $FeCl_3$–activated carbon system is an excellent catalyst for the reduction of aromatic and heterocyclic nitro compounds by hydrazine hydrate to give amines. This system was first proposed by Hirashima and Manare [7] in 1975, but has not found common use in organic synthesis.

The catalyst is generated *in situ* by the addition of $N_2H_4 \cdot H_2O$ to a suspension of activated carbon, containing $FeCl_3$, in aqueous ethanol. The major advantages of this method are the availability, high activity, and stability in relation to the catalyst poisons and the lack of ferric ion impurities in the reaction mixtures.

In the present work, we attempted to extend the scope of application of the $FeCl_3$–C_{act}–$N_2H_4 \cdot H_2O$ system in synthesis and to use it for obtaining indoles by the Leimgruber-Batcho synthesis.

The starting 2-methyl-1-nitrobenzenes **1a–n** were converted to enamines **2a–g,i–l** (Table 1) by treating with DMF dimethyl acetal in the presence of pyrrolidine in dry DMF. Products **2h,m,n** were obtained without the addition of pyrrolidine.

In order to carry out the subsequent reduction, it was very important to keep the enamines separate from the reaction side products, especially, nonvolatile N-formylpyrrolidine. As a rule, products **2** crystallize from the reaction mixture and may thus be readily separated. Further purification by recrystallization was not carried out.



1, 2 a R = 4-MeO, **b** R = 4-BnO, **c** R = 4-*i*-PrO, **d** R = 4-(4-$FC_6H_4CH_2O$), **e** R = 4-(3,4-$Cl_2C_6H_3CH_2O$), **f** R = 3-Cl, **g** R = 5-(2,5-$Me_2C_4H_2N$), **h** R = 4-(CF_2HO), **i** R = 4-(CF_2HCH_2O), **j** R = 4-($CF_2HCF_2CH_2O$), **k** R = 5-Me, **l** R = 5-MeO, **m** R = 5-Br, **n** R = 5-Cl; **2 a–g**, **i–l** $R^1+R^2 = -(CH_2)_4-$, **h,m,n** $R^1 = R^2$ = Me

TABLE 1. Yields, Reagent Ratios and Reaction Conditions

Compound	DMF dimethyl acetal/ substrate ratio, mol/mol	Temperature, °C	Time, h	Yield, %
2a	1.2	110	5	65
2b	1.2	110	5	86
2c	1.2	110	5	85
2d	1.1	100	8	82
2e	1.1	100	8	77
2f	1.2	110	8	61
2g	1.2	110	10	86
2h	1.2*	110	10	55
2i	1.1	95	10	72
2j	1.1	100	10	74
2k	1.3	100	8	63
2l	1.2	115	20	55
2m	1.5*	115	20	63
2n	1.5*	115	20	73

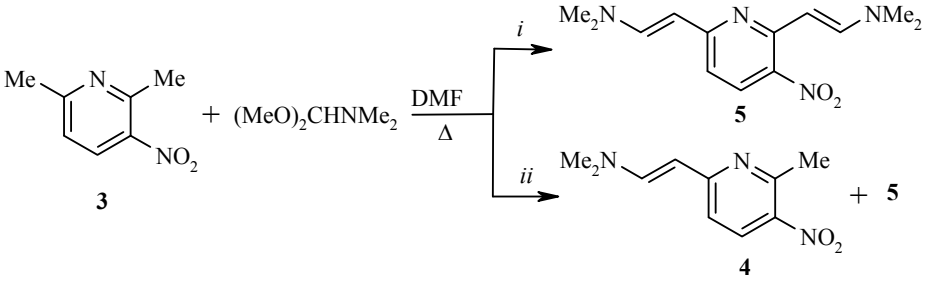
***** Without the addition of pyrrolidine. The yield was calculated relative to the NMe_2 derivative.

For substrates tending to undergo nucleophilic aromatic substitution such as 5-halo-2-methyl-1-nitrobenzenes (**1m,n**), the replacement of the halogen atom by pyrrolidine may compete with enamine formation. In this case, pyrrolidine is not added but the reaction time is considerably extended.

Enamines **2** are moderately stable dark-red compounds. ^{1}H NMR spectroscopy shows that these products consist of varying amounts of (*E*)-β-(pyrrolidino)- and (*E*)-β-(N,N-dimethylamino)nitrostyrenes. The usual content of the (N,N-dimethylamino)styrene impurity is 2–10%, but this by-product does not hinder further reduction and needs not to be separated.

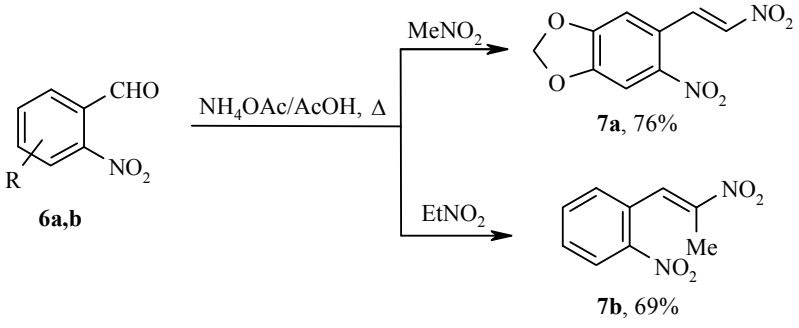
We should note that enamines **2** decompose upon prolonged storage at room temperature and are also unstable on silica gel, which makes their chromatographic purification impossible and hinders monitoring of the reaction course by thin-layer chromatography.

We also studied the feasibility of using this method for the synthesis of an azaindole (1H-pyrrolo-[3,2-*b*]pyridine), for which relatively available 2,6-dimethyl-3-nitropyridine (**3**) was taken as the starting compound. The reaction of nitropyridine **3** with DMF dimethyl acetal (without the addition of pyrrolidine) by a reagent ratio of 1:1.3 leads to a 7:3 mixture of enamines **4** and **5** as indicated by ^{1}H NMR spectroscopy. This result corresponds to the data of Dallacker [8] on the relative activity of the methyl groups in pyridine **3**. Unfortunately, we could not separate products **4** and **5**. Only the bis-derivative **5** was formed when the reagent ratio was 1:3.



i 1:3, 110 °C, 15 h, 75%; *ii* 1:1.3, 110°C, 10 h

Finally, we studied compounds, which were structurally similar to enamines **2**, namely, 2-nitro-β-nitrostyrenes **7a,b,** obtained by the condensation of substituted 2-nitrobenzaldehydes **6a,b** with nitromethane [8] and nitroethane [9], respectively.



6 a R = 1,2-(–OCH_2O–), **b** R = H

The reduction and cyclization of all synthesized products was carried out under similar conditions. The reagent ratio was 5 mol% $FeCl_3 \cdot 6H_2O$, 20 mol% highly dispersed activated carbon, and 10 mol $N_2H_4 \cdot H_2O$ per mol substrate containing one nitro group. Ethanol or 2-propanol in an amount sufficient to dissolve the starting nitro compound was used as the solvent.

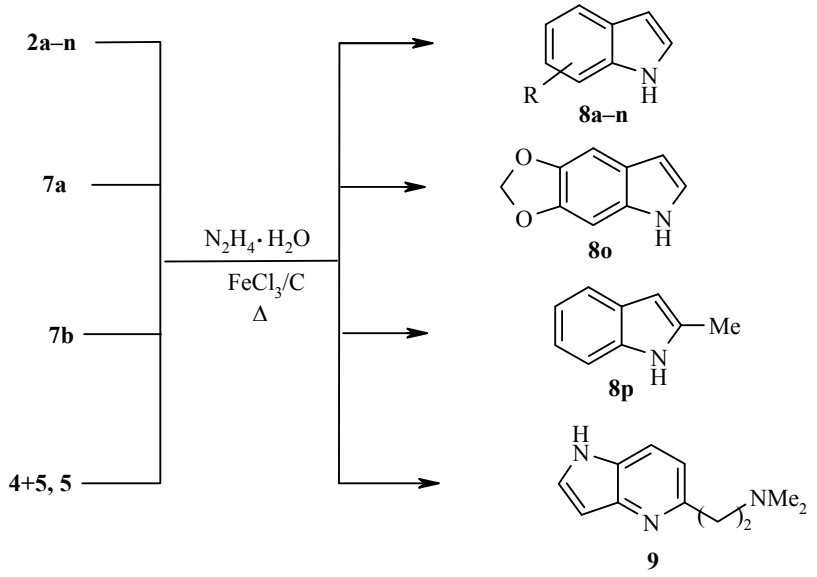
The order of mixing of the reagents is a determining factor for the success of the reaction. The best results were obtained using the following method. The catalyst was initially prepared by adding highly dispersed carbon into a solution of $FeCl_3 \cdot 6H_2O$ with vigorous stirring and then the entire amount of hydrazine hydrate was added dropwise. The mixture was heated to approximately 50°C. The nitro compound as a dry solid or in solution was added in small portions to the suspension obtained and heated for 2–10 h until the end of the reaction.

The treatment of the reaction mixture is extremely simple. The catalyst is filtered off and the solvent is removed in vacuum. The residue is purified by suitable method. The yields, as a rule, are high (Table 2).

This method places a number of limitations on the structure of the substrate. Thus, compounds containing CN, CO_2R, CO_2H, COR, $CONH_2$, and some other groups cannot be reduced using this method. 2-Nitro-β-nitrostyrenes **7a,b** are reduced in moderate yield comparable to the yields obtained when using other reducing agents [9].

The reduction of pyridine derivatives **4** and **5** should be discussed separately. It was assumed that the reduction of the double bond in the side chain could occur. In test experiments, a mixture of compounds **4** and **5** was subjected to reduction.

Analysis of the ^{1}H NMR spectra of the reaction mixtures showed that such reduction indeed proceeds but only about 10% of the desired product **9** is present. All attempts to isolate this product by chromatography proved unsuccessful.



8a R =5-MeO, **b** R = 5-BnO, **c** R = 5-*i*-PrO, **d** R = 5-(4-$FC_6H_4CH_2O$), **e** R = 5-(3,4-$Cl_2C_6H_3CH_2O$), **f** R = 4-Cl, **g** R = 6-(2,5-$Me_2C_4H_2N$), **h** R = 5-(CF_2HO), **i** R = 5-(CF_2HCH_2O), **j** R = 5-($CF_2HCF_2CH_2O$), **k** R = 6-Me, **l** R = 6-MeO, **m** R = 6-Br, **n** R = 6-Cl

The ^{1}H NMR spectrum analysis of the reaction mixtures in the reduction of pure nitropyridine derivative **5** showed that the content of azaindole **9** was about 40%, but the isolated yield was only 12% after chromatography and crystallization. The physical constants and spectral data of azaindole **9** sample obtained by us correspond to literature values [9]. The conditions used in this work are probably not suitable for the preparation of azaindole derivatives.

Thus, the $FeCl_3$–C_{act}–$N_2H_4 \cdot H_2O$ system can serve as a convenient addition to the set of reducing agents used for the preparation of indoles by the Leimgruber–Batcho method. The scope of this method is currently under study.

EXPERIMENTAL

The ^{1}H, ^{19}F, and ^{13}C NMR spectra were taken on a Bruker AC-300 spectrometer at 300, 283, and 50 MHz, respectively, and AC-200 spectrometer at 200 MHz (for ^{1}H NMR spectra only) at 25°C. The solvents were: $CDCl_3$ for **1d,e,g–j, 2a–n, 5, 8a–c,f–n,p**, DMSO-d_6 for **8d,e,o**, and CD_3OD for **9**. TMS was used as the internal standard for the ^{1}H and ^{13}C NMR spectra, while $CFCl_3$ was used as the external standard for the ^{19}F NMR spectra. The electron impact mass spectra were taken on a Finnigan Incos 50 mass spectrometer with direct inlet of the sample into the ion source at 70 eV. Thin-layer chromatography was carried out on Merck Silica Gel $60F_{256}$ plates with detection by UV light. Column chromatography was carried out using Merck silica gel 60 (fraction 0.06–0.2 mm). The melting points were determined in open capillaries using a Schorpp MRM-1HV instrument manufactured in Germany.

DMF dimethyl acetal and pyrrolidine obtained from Acros Organics, Belgium, were used without further purification. A high-purity sample of DMF was distilled over CaH_2 in vacuum and stored over 4 Å molecular sieves prior to use. Norit SA2 activated carbon powder from Acros was used without further treatment.

Nitrobenzenes **1a** [12], **1b** [13], and **1c** [14] were prepared by reported procedures. Substituted *o*-methylnitrobenzenes **1h–j** were obtained from ArtChem Gmbh (Berlin-Buch, Germany), while **1f,k–p** were obtained from Sigma-Aldrich (USA).

4-(Difluoromethoxy)-2-methyl-1-nitrobenzene (1h), mp 30–30.5°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.05 (1H, d, *J* = 8.1, H Ar); 7.05 (2H, m, H Ar); 6.65 (1H, t, *J* = 52.7, HCF_2); 2.65 (3H, s, CH_3). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –83.2 (2F, d, *J* = 73.0). Mass spectrum, *m/z* (I_{rel}, %): 203 $[M]^+$ (17), 186 (64), 136 $[M–OCF_2H]^+$ (35), 51 $[HCF_2]^+$ (100).

4-(2,2-Difluoroethoxy)-2-methyl-1-nitrobenzene (1i), mp 32–33°C, bp 160–162°C (6 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.1 (1H, d, *J* = 8.1, H Ar); 6.85 (2H, m, H Ar); 6.15 (1H, tt, J_1 = 40.5, J_2 = 4.4, HCF_2); 4.25 (2H, td, J_1 = 8.0, J_2 = 4.4, $C\underline{H_2}CHF_2$); 2.65 (3H, s, CH_3). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –126.3 (2F, dt, J_1 = 55.0, J_2 = 14.3). Mass spectrum, *m/z* (I_{rel}, %): 277 $[M]^+$ (52), 200 (100), 136 $[M–OCH_2CF_2H]^+$ (34), 65 $[CH_2HCF_2]^+$ (100), 51 $[HCF_2]^+$ (79).

2-Methyl-1-nitro-4-(2,2,3,3-tetrafluoropropoxy)benzene (1j), bp 138–140°C (4 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.1 (1H, d, *J* = 8.1, H Ar); 6.85 (2H, m, H Ar); 6.05 (1H, m, HCF_2); 4.45 (2H, t, *J* = 8.0, CH_2CF_2); 2.65 (3H, s, CH_3). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –125.6 (2F, s, CF_2), –139.7 (2F, d, *J* = 55.0, CHF_2). Mass spectrum, *m/z* (I_{rel}, %): 267 $[M]^+$ (18), 250 (43), 136 $[M–OCH_2CF_2CF_2H]^+$ (10), 51 $[HCF_2]^+$ (100).

Nitrobenzenes 1d and 1e (**General Method**). Potassium carbonate (13.8 g, 100 mmol) was added to a solution of 3-methyl-4-nitrophenol (15.3 g, 100 mmol) in DMF (90 ml) and heated to 50°C. Corresponding benzyl chloride (110 mmol) was slowly added at this temperature. The temperature was raised to 100°C and the mixture was stirred for an additional 3 h. At the end of the reaction, the mixture was cooled and poured with vigorous stirring into 500 ml of ice water. The precipitate formed was filtered off, washed on the filter with water, and dried.

4-[(4-Fluorobenzyl)oxy]-2-methyl-1-nitrobenzene (1d) was obtained in 84% yield; mp 101–102°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.10 (1H, m, H Ar); 7.45 (2H, m, H Ar); 7.10 (2H, m, H Ar); 6.85 (2H, m, H Ar); 5.10 (2H, s, CH_2); 2.65 (3H, s, CH_3). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –114.1 (1F, s). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 164.3; 162.0; 161.0; 142.4; 137.0; 131.6 (d, *J* = 3.3); 129.5 (d, *J* = 8.3); 127.5; 118.3; 115.7 (d, *J* = 21.0); 112.5; 69.8; 21.6. Found, %: C 64.38; H 4.69; N 5.41. $C_{14}H_{12}FNO_3$. Calculated, %: C 64.36; H 4.63; N 5.36.

1,2-Dichloro-4-[(3-methyl-4-nitrophenoxy)methyl]benzene (1e) was obtained in 91% yield; mp 135–136°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm: 8.1 (1H, m, H Ar); 7.50 (2H, m, H Ar); 7.25 (1H, m, H Ar); 6.85 (2H, m, H Ar); 5.1 (2H, m, CH_2); 2.65 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 161.5; 142.6; 137.0; 136.0; 133.0; 132.3; 130.5; 129.2; 127.5; 126.5; 118.4; 112.5; 68.8; 21.6. Found, %: C 54.08; H 3.77; N 4.63. $C_{14}H_{11}Cl_2NO_3$. Calculated, %: C 53.87; H 3.55; N 4.49.

2,5-Dimethyl-1-(4-methyl-3-nitrophenyl)-1H-pyrrole (1g). A solution of 4-methyl-3-nitroaniline (13.7 g, 90 mmol) and 2,5-hexanedione (11.7 ml, 100 mmol, 11.4 g) in AcOH (150 ml) was heated for 2 h at 110°C. The solvent was removed under reduced pressure (10 mmHg, bath temperature 50°C) and the residue was poured into 10% aqueous sodium carbonate (250 ml). The precipitate formed was filtered off, dissolved in ether, and dried over magnesium sulfate. The solution was evaporated until the crystallization began. An equal volume of hexane was added. The mixture was cooled and the precipitate was filtered off to give 18.3 g (88%) compound **1g** as yellow crystals; mp 93–94°C. ^{1}H NMR spectrum, δ, ppm: 7.90 (1H, s, H Ar); 7.55 (1H, m, H Ar); 7.40 (1H, m, H Ar); 5.95 (2H, s, CH pyrrole); 2.70 (3H, s, CH_3); 2.10 (6H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 149.1; 146.9; 133.5; 132.6; 131.9; 127.6; 123.3; 106.5; 18.9; 12.6. Mass spectrum, *m/z* (I_{rel}, %): 230 $[M]^+$ (100), 184 $[M–NO_2]^+$ (28). Found, %: C 69.18; H 6.17; N, 12.42. $C_{13}H_{14}N_2O_2$ Calculated, %: C 67.81; H 6.13; N 12.17.

Enamines 2 (**General Method**). A solution of *o*-methylnitrobenzene **1** (50 mmol), DMF dimethyl acetal (7.8 ml, 7 g, 60 mmol), and pyrrolidine (4.9 ml, 60 mmol), 4.2 g in DMF (40 ml) was heated in a nitrogen atmosphere under conditions indicated in Table 1 (the reagent ratio was 1:1.2:1.2; in other cases, we took either more or less of the reagents). Pyrrolidine was not added in the syntheses of **2h,m,n, 4,** and **5**. Then, the volatile compounds were removed from the hot mixture in vacuum (10 mmHg, bath temperature 90°C). The residue was mixed with hot methanol (50 ml). Crystallization may start immediately or after some time. The mixture containing the crystals was maintained for an additional 3 h at 0°C. The precipitate was filtered off and washed on the filter with a small amount of methanol cooled to –20°C. The product was dried in vacuum and stored at –18°C in a closed dark container. The product was used for the reduction without further purification. The ^{1}H NMR spectra of these products show only signals for the major compound.

1-[(*E*)-2-(5-Methoxy-2-nitrophenyl)vinyl]pyrrolidine (2a), mp 67–68°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.95 (1H, d, *J* = 7.5, H Ar); 7.25 (1H, d, *J* = 7.5, H Ar); 6.85 (1H, s, H Ar); 6.50 (1H, m, CH=); 6.05 (1H, d, *J* = 11.0, CH=); 3.85 (3H, s, OCH_3); 3.35 (4H, m, pyrrolidine); 2.0 (4H, m, CH_2 pyrrolidine).

TABLE 2. Reaction Conditions and Yields of Indole Derivatives

Compound	Solvent	Temperature, °C	Time, h	Yield, %
8a	EtOH	75	5	91
8b	2-PrOH	80	5	95
8c	EtOH	75	5	85
8d	2-PrOH	80	8	77
8e	2-PrOH	80	8	79
8f	EtOH	75	5	32
8g	2-PrOH	80	5	86
8h	EtOH	75	3	58
8i	EtOH	75	3	72
8j	EtOH	75	3	92
8k	EtOH	75	5	81
8l	EtOH	75	7	93
8m	EtOH	75	7	93
8n	EtOH	75	7	96
8o	2-PrOH	80	5	37
8p	2-PrOH	80	5	41
9*	2-PrOH	80	10	10*[2]
9	2-PrOH	80	15	12

* Reduction of a mixture of **4** and **5**.

*[2] According to the ^{1}H NMR spectrum. Product **9** was not isolated.

1-[(*E*)-2-(5-Benzyloxy-2-nitrophenyl)vinyl]pyrrolidine (2b), mp 96–97°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.75 (1H, d, *J* = 12.1, H Ar); 7.25 (6H, m, H Ar); 6.9 (2H, m, H Ar + CH=); 5.20 (1H, d, *J* = 12.1, CH=); 5.00 (2H, s, CH_2); 3.10 (4H, m, CH_2 pyrrolidine); 1.80 (4H, m, CH_2 pyrrolidine).

1-[(*E*)-2-(5-Isopropoxy-2-nitrophenyl)vinyl]pyrrolidine (2c) crystallized upon maintenance for 24 h at 0°C; mp 59–60°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.95 (1H, d, *J* = 8.0, H Ar); 7.20 (1H, d, *J* = 11.2, H Ar); 6.85 (1H, s, H Ar); 6.50 (1H, d, *J* = 8.5, CH=); 6.05 (1H, d, *J* = 11.2, CH=); 4.65 (1H, q, *J* = 6.0, CH); 3.35 (4H, m, CH_2 pyrrolidine); 1.95 (4H, m, CH_2 pyrrolidine); 1.45 (6H, d, *J* = 6.0, CH_3).

1-{(*E*)-2-[5-(4-Fluorobenzyl)oxy-2-nitrophenyl]vinyl}pyrrolidine (2d) crystallized upon maintenance for 24 h at 0°C; mp 93–94°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.54 (3H, m, H Ar); 7.13 (2H, m, H Ar); 6.80 (1H, m, H Ar); 6.75 (1H, d, *J* = 8.4, CH=); 6.61 (1H, m, H Ar); 6.05 (1H, d, *J* = 11.1, CH=); 5.05 (2H, s, CH_2); 3.39 (4H, m, CH_2 pyrrolidine); 2.10 (4H, m, CH_2 pyrrolidine). ^{19}F NMR spectrum, δ, ppm: –115.8 (1F, s).

1-{(*E*)-2-[5-(3,4-Dichlorobenzyl)oxy]-2-nitrophenyl]vinyl}pyrrolidine (2e), mp 68–70°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.90 (1H, d, *J* = 7.5, H Ar); 7.50 (2H, m, H Ar); 7.30 (2H, m, H Ar); 6.90 (1H, s, H Ar), 6.50 (1H, m, CH=); 6.00 (1H, d, *J* = 11.2, CH=); 5.05 (2H, s, CH_2); 3.35 (4H, m, CH_2 pyrrolidine); 2.00 (4H, m, CH_2 pyrrolidine).

1-[(*E*)-2-(2-Chloro-6-nitrophenyl)vinyl]pyrrolidine (2f) was obtained as a viscous, noncrystalline oil; bp 111°C (0.03 mmHg) [4]. Decomposes at higher pressure. The purity of the sample, as indicated by ^{1}H NMR spectroscopy, was 70%. The sample was used without further purification. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.2 (1H, m, H Ar); 7.35 (2H, m, H Ar); 6.7 (1H, d, *J* = 9.0, CH=); 5.2 (1H, d, *J* = 9.0, CH=); 3.4 (4H, m, CH_2 pyrrolidine); 2.1 (4H, m, CH_2 pyrrolidine).

2,5-Dimethyl-1-{3-nitro-4-[(*E*)-2-pyrrolidin-1-ylvinyl]phenyl}-1H-pyrrole (2g), mp 103–105°C (decomp.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.80 (1H, s, H Ar); 7.55 (2H, d, *J* = 11.0, H Ar); 7.45 (1H, d, *J* = 16.0, CH=); 5.90 (3H, s, =CH + CH pyrrole); 3.4 (4H, m, CH_2 pyrrolidine); 2.10 (6H, s, CH_3); 2.00 (4H, m, CH_2 pyrrolidine).

(*E*)-2-(5-Difluoromethoxy-2-nitrophenyl)-N,N-dimethylethyleneamine (2h), mp 65–68°C. The corresponding derivative with pyrrolidine is liquid at room temperature. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.90 (1H, d, *J* = 9.2, H Ar); 7.10 (1H, s, H Ar); 6.95 (1H, d, *J* = 9.2, H Ar); 6.65 (1H, d, *J* = 13.8, CH=); 6.57 (1H, t, *J* = 72.8, HCF_2); 5.90 (1H, d, *J* = 13.8, CH=); 2.95 (6H, s, $N(CH_3)_2$). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –82.2 (2F, d, *J* = 74.0).

1-{(*E*)-2-[5-(2,2-Difluoroethoxy)-2-nitrophenyl]vinyl}pyrrolidine (2i), mp 128–129°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.95 (1H, d, *J* = 10.0, H Ar); 7.25 (1H, m, CH=); 6.87 (1H, m, H Ar); 6.48 (1H, m, H Ar); 6.12 (1H, tm, J_1 = 57.0, HCF_2); 6.05 (1H, m, CH=); 4.23 (2H, td, J_1 = 12.9, J_2 = 3.9, $C\underline{H_2}CHF_2$); 3.35 (4H, m, CH_2 pyrrolidine); 1.96 (4H, m, CH_2 pyrrolidine). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –126.2 (2F, dt, J_1 = 56.0, J_2 = 14.2).

1-{(*E*)-2-[2-Nitro-5-(2,2,3,3-tetrafluoropropoxy)phenyl]vinyl}pyrrolidine (2j), mp 106–107°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.95 (1H, d, *J* = 9.2, H Ar); 7.25 (1H, d, *J* = 13.1, CH=); 6.87 (1H, s, H Ar); 6.47 (1H, m, H Ar); 6.3–5.8 (2H, m, CH= + CHF_2); 4.40 (2H, t, *J* = 11.2, CH_2F_2); 3.35 (4H, m, CH_2 pyrrolidine), 1.96 (4H, m, CH_2 pyrrolidine). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –125.6 (2F, s); –139.7 (2F, d, *J* = 54.4).

1-[(*E*)-2-(4-Methyl-2-nitrophenyl)vinyl]pyrrolidine (2k), mp 69–70°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.70 (1H, s, H Ar); 7.35 (1H, m, H Ar); 7.20 (2H, m, HAr + CH=); 5.80 (1H, d, *J* = 12.0, CH=); 3.30 (4H, m, CH_2 pyrrolidine); 2.30 (3H, s, CH_3); 2.00 (4H, m, CH_2 pyrrolidine).

1-[(*E*)-2-[4-Methoxy-2-nitrophenyl)vinyl]pyrrolidine (2l) was obtained as a dark-red semiliquid at room temperature, which precipitates as crystals from cold methanol and may be separated by filtration on an ice-cooled funnel. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.40 (2H, m, H Ar); 7.10 (1H, d, *J* = 12.2, CH=); 6.95 (1H, m, H Ar); 5.85 (1H, d, *J* = 12.2, CH=); 3.80 (3H, s, OCH_3); 3.35 (4H, m, CH_2 pyrrolidine); 1.95 (4H, m, CH_2 pyrrolidine).

(*E*)-2-(4-Bromo-2-nitrophenyl)-N,N-dimethylethyleneamine (2m), mp 81–82°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.98 (1H, s, H Ar); 7.32 (2H, m, H Ar); 6.95 (1H, m, H Ar); 6.05 (1H, d, *J* = 13.1, CH=); 5.80 (1H, d, *J* = 13.1, CH=); 2.92 (6H, s, $N(CH_3)_2$).

(*E*)-2-(4-Chloro-2-nitrophenyl)-N,N-dimethylethyleneamine (2n), mp 51–52°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.85 (1H, s, H Ar); 7.30 (2H, m, H Ar); 6.95 (1H, d, *J* = 13.2, CH=); 5.83 (1H, d, *J* = 13.8, CH=); 2.92 (6H, s, $N(CH_3)_2$).

(*E,E*)-2,2'-(3-Nitropyridine-2,6-diyl)bis(N,N-dimethylethyleneamine) (5), mp 129–131°C (mp 131°C [11]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.97 (1H, d, *J* = 13.9, CH=); 7.95 (1H, d, *J* = 14.0, CH=); 7.50 (1H, d, *J* = 13.9, H Ar); 6.33 (1H, d, *J* = 14.0, H Ar); 6.31 (1H, d, *J* = 8.9, CH=); 5.10 (1H, d, *J* = 13.9, CH=); 2.95 (6H, s, $N(CH_3)_2$); 2.9 (6H, s, $N(CH_3)_2$).

Indoles 8 and 9 (**General Method**). Activated carbon powder (1.7 g) was added to a solution of $FeCl_3 \cdot 6H_2O$ (1.1 g, 4.1 mmol) in alcohol (ethanol or 2-propanol) (100 ml) and heated with stirring at 40–50°C. 100% hydrazine hydrate (48.5 ml, 50.2 g, 1 mol) was added at this temperature and the mixture was maintained for 0.5 h. Then, enamine **2** (100 mmol) was added in small portions at a rate such that the temperature did not exceed 70°C and gas liberation was not too vigorous. After addition of the substrate, the mixture was heated at reflux for 2–10 h until the reaction was complete as indicated by thin-layer chromatography. The mixture was cooled. The precipitate was removed and the solvent was distilled off in vacuum. The residue was either distilled or recrystallized.

5-Methoxy-1H-indole (8a), bp 148–150°C (4–5 mmHg), mp 55–56°C (ligroin). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.96 (1H, br. s, NH); 7.17 (1H, d, *J* = 8.3, H Ar); 7.07 (2H, m, H Ar); 6.85 (1H, m, H Ar); 6.40 (1H, m, CH pyrrole); 3.82 (3H, s, OCH_3).

5-(Benzyloxy)-1H-indole (8b), mp 99–102°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm: 7.90 (1H, br. s, NH); 7.45 (2H, m, H Ar); 7.35 (3H, m, H Ar); 7.16 (2H, m, H Ar); 7.02 (1H, m, H Ar); 6.42 (1H, m, CH pyrrole); 5.06 (2H, s, CH_2).

5-Isopropoxy-1H-indole (8c), bp 136–137°C (2 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.16 (1H, br. s, NH); 7.22 (3H, m, H Ar); 6.92 (1H, m, H Ar); 6.51 (1H, s, CH pyrrole); 4.58 (1H, m, $CHMe_2$); 1.42 (6H, d, *J* = 6.0, CH_3). ^{13}C NMR spectrum, δ, ppm: 151.9; 131.3; 128.4; 125.1; 114.3; 111.8; 106.6; 102.1; 71.7; 22.2. Mass spectrum, *m/z* (I_{rel}, %): 175 $[M]^+$ (25), 133 $[M–i\text{-}Pr]^+$ (100). Found, %: C 75.43; H 7.56; N 8.12. $C_{11}H_{13}NO$. Calculated, %: C 75.40; H 7.48; N 7.99.

5-[(4-Fluorobenzyl)oxy]-1H-indole (8d), mp 130.0–130.5°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.95 (1H, br. s, NH); 7.49 (2H, m, H Ar); 7.20 (5H, m, H Ar + CH pyrrole); 6.81 (1H, d, *J* = 11.2, H Ar); 6.33 (1H, s, CH pyrrole); 5.05 (2H, s, CH_2). ^{19}F NMR spectrum, δ, ppm: –115.6 (1F, s). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 163.0; 160.1; 152.2; 131.0; 129.6 (d, *J* = 8.6); 128.2; 125.7; 115.0 (d, *J* = 8.6); 111.9; 111.7; 103.4; 100.9; 69.1. Mass spectrum, *m/z* (I_{rel}, %): 241 $[M]^+$ (50), 132 $[M–4\text{-F-Bz}]^+$ (83), 109 $[4\text{-F-Bz}]^+$ (100). Found, %: C 74.51; H 5.12; N 5.90. $C_{15}H_{12}FNO$. Calculated, %: C 74.67; H 5.01; N 5.81.

5-[(3,4-Dichlorobenzyl)oxy]-1H-indole (8e), mp 120.5–121°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.96 (1H, br. s, NH); 7.63 (2H, m, H Ar); 7.42 (1H, d, *J* = 7.9, CH pyrrole); 7.28 (2H, m, H Ar); 7.10 (1H, s, H Ar); 6.80 (1H, d, *J* = 11.8, H Ar); 6.32 (1H, s, CH pyrrole); 5.09 (2H, s, CH_2). ^{13}C NMR spectrum, δ, ppm: 151.8; 139.0; 131.3; 131.0; 130.4; 129.1; 127.9; 127.4; 125.9; 112.0; 111.7; 103.5; 100.9; 68.2. Mass spectrum, *m/z* (I_{rel}, %): 292 $[M]^+$ (13), 132 $[M–H–3,4\text{-}Cl_2Bz]^+$ (21), 131 $[M–H–3,4\text{-}Cl_2Bz]^+$ (100), 104 (61). Found, %: C 61.59; H 3.56; N 4.71. $C_{15}H_{11}Cl_2NO$. Calculated, %: C 61.67; H 3.79; N 4.79.

4-Chloro-1H-indole (8f) was separated on a silica gel column using 3:2 v/v CH_2Cl_2–hexane as the eluent and then distilled in vacuum; bp 129–131°C (4–5 mmHg). ^{1}H NMR spectrum, δ, ppm: 8.15 (1H, br. s, NH); 7. 25 (1H, m, H Ar); 7.1 (2H, m, H Ar + CH pyrrole); 6.64 (1H, m, CH pyrrole).

6-(2,5-Dimethyl-1H-pyrrol-1-yl)-1H-indole (8g), mp 188–189°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm: 8.28 (1H, br. s, NH); 7.70 (1H, m, CH); 7.27 (3H, m, H Ar); 6.96 (1H, m, CH); 6.65 (1H, s, CH); 5.59 (2H, s, H pyrrole); 2.06 (6H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 135.7; 131.8; 127.8; 127.0; 126.6; 120.3;

119.2; 110.8; 105.1; 101.1; 12.8. Mass spectrum, *m/z* (I_{rel}, %): 210 $[M]^+$ (100), 209 $[M–H]^+$ (67), 154 (35). Found, %: C 80.09; H 6.57; N 13.51. $C_{14}H_{14}N_2$. Calculated, %: C 79.97; H 6.71; N 13.32.

5-(Difluoromethoxy)-1H-indole (8h), bp 116–117°C (2 mmHg). This product darkens rapidly in the air at room temperature and should be stored at –18°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.23 (1H, br. s, NH); 7.35 (3H, m, CH); 7.04 (1H, d, *J* = 8.5, CH); 7.57 (1H, s, CH); 6.53 (1H, t, *J* = 74.8, CHF_2). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –80.1 (1F, d, *J* = 75.0). ^{13}C NMR spectrum, δ, ppm: 133.6; 128.3; 126.0; 120.5; 120.0; 115.3; 113.7; 111.9; 111.4; 102.8. Mass spectrum, *m/z* (I_{rel}, %): 183 $[M]^+$ (100), 132 $[M–H\text{-}R_F]^+$ (73), 104 $[C_8H_8]^+$ (60), 51 $[HCF_2]^+$ (40). Found, %: C 59.19; H 3.99; N 7.31. $C_9H_7F_2NO$. Calculated, %: C 59.02; H 3.85; N 7.65.

5-(2,2-Difluoroethoxy)-1H-indole (8i), bp 141–142°C (2 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.08 (1H, br. s, NH); 7.30 (1H, d, *J* = 9.2, CH); 7.19 (2H, s, CH); 6.95 (1H, m, CH); 6.55 (1H, s, CH); 6.14 (1H, tt, J_1 = 55.2, J_2 = 4.6, CHF_2); 4.25 (2H, td, J_1 = 13.8, J_2 = 3.9, $C\underline{H}_2CHF_2$). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –125.8 (1F, dt, J_1 = 56.0, J_2 = 15.0). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 152.3; 131.6; 125.5; 125.1; 117.2; 114.0; 112.4; 112.0 (t, J_1 = 12.4, J_2 = 8.6); 104; 102.2 (t, J_1 = 18.3, J_2 = 6.2); 68.3 (t, *J* = 28.3). Mass spectrum, *m/z* (I_{rel}, %): 197 $[M]^+$ (72), 132 $[M–H\text{-}R_F]^+$ (100), 104 $[C_8H_8]^+$ (67), 77 (20), 51 $[HCF_2]^+$ (20). Found, %: C 61.13; H 4.34; N 7.19. $C_{10}H_9F_2NO$. Calculated, %: C 60.91; H 4.60; N 7.10.

5-(2,2,3,3-Tetrafluoropropoxy)-1H-indole (8j), mp 64–66°C (heptane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.13 (1H, br. s, NH); 7.24 (3H, m, CH); 6.90 (1H, d, *J* = 8.6, CH); 6.52 (1H, s, CH); 6.15 (1H, tt, J_1 = 53.2, J_2 = 5.2, CHF_2); 4.40 (2H, t, *J* = 11.8, CH_2CF_2). ^{19}F NMR spectrum, δ, ppm: –126.1 (2F, s, CF_2); –140.4 (2F, d, *J* = 59.0, CHF_2). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 152.2; 131.9; 128.3; 125.6; 118.0 (t, J_1 = 28.0); 114.9 (t, J_1 = 28.0); 112.5; 112.1 (m); 109.3 (t, J_1 = 35.0); 105.9 (t, J_1 = 35.0); 104.7; 102.5; 66.8 (t, *J* = 31.0). The resolved signals belong to the carbon atoms of the $\underline{C}HF_2\underline{C}F_2$ fragment and are a superposition of two triplets of triplets with J_2 = 250.0 Hz. Mass spectrum, *m/z* (I_{rel}, %): 247 $[M]^+$ (77), 132 $[M–H\text{-}R_F]^+$ (100), 104 $[C_8H_8]^+$ (55), 51 $[HCF_2]^+$ (25). Found, %: C 53.21; H 3.79; N 5.61. $C_{11}H_9F_4NO$. Calculated, %: C 53.45; H 3.67; N 5.67.

6-Methyl-1H-indole (8k), bp 112–113°C (4–5 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.65 (1H, br. s, NH); 7.52 (1H, d, *J* = 8.1, H Ar); 6.95 (3H, m, H Ar + CH pyrrole); 6.46 (1H, m, CH pyrrole); 2.45 (3H, s, CH_3).

6-Methoxy-1H-indole (8l), mp 95.0–95.5°C (from heptane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.03 (1H, br. s, NH); 7.55 (1H, d, *J* = 8.5, H Ar); 7.10 (1H, s, H Ar); 6.86 (2H, m, H Ar); 6.51 (1H, s, H Ar); 3.87 (3H, s, OCH_3). Mass spectrum, *m/z* (I_{rel}, %): 147 $[M]^+$ (100), 132 $[M–CH_3]^+$ (100), 104 $[C_8H_8]^+$ (49).

6-Bromo-1H-indole (8m), mp 96–97°C (heptane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.13 (1H, br. s, NH); 7.53 (2H, m, H Ar); 7.24 (2H, m, H Ar); 6.55 (1H, s, H Ar). Mass spectrum, *m/z* (I_{rel}, %): 197 $[M, Br^{81}]^+$ (97), 195 $[M, Br^{79}]^+$ (100), 116 $[M–Br]^+$ (88), 89 $[M–Br–HCN]^+$ (43).

6-Chloro-1H-indole (8n), mp 92.0–92.5°C (heptane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.05 (1H, br. s, NH); 7.57 (1H, d, *J* = 7.9, H Ar); 7.35 (1H, s, H Ar); 7.14 (2H, m, H Ar); 6.55 (1H, s, H Ar). Mass spectrum, *m/z* (I_{rel}, %): 153 $[M, Cl^{37}]^+$ (32), 151 $[M, Cl^{35}]^+$ (100), 116 $[M–Cl]^+$ (17), 89 $[M–Cl–HCN]^+$ (30).

5H-[1,3]Dioxolo[4,5-*f*]indole (8o), mp 107–109°C (aqueous ethanol). ^{1}H NMR spectrum, δ, ppm: 8.65 (1H, br. s, NH); 7.20 (2H, m, H Ar); 6.95 (1H, s, H Ar); 6.45 (1H, m, ArH); 5.85 (2H, s, OCH_2O).

2-Methyl-1H-indole (8p), mp 56–58°C (hexane). ^{1}H NMR spectrum, δ, ppm: 7.48 (1H, m, H Ar); 7.42 (1H, br. s, NH); 7.09 (3H, m, H Ar + CH pyrrole); 6.16 (1H, m, CH pyrrole); 2.28 (3H, s, CH_3).

(*E*)-N,N-Dimethyl-2-(1H-pyrrolo[3,2-*b*]pyridine-5-yl)ethaneamine (9) was isolated by chromatography on a silica gel column using ethyl acetate-methanol (9:1) as the eluent and crystallized from hexane−ethyl acetate, mp 173–174°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.21 (1H, d, *J* = 8.9, H Ar); 7.90 (1H, m, H Ar); 7.53 (1H, d, *J* = 8.9, H Ar); 6.90 (1H, m, H Ar); 3.90 (2H, m, CH_2); 3.65 (2H, m, CH_2); 3.00 (6H, s, $N(CH_3)_2$).

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