Synthesis of Substituted Nitrooxindoles via Intramolecular Oxidative Nucleophilic Substitution of Hydrogen in *m*-Nitroacylanilides

Mieczysław Mąkosza,* Maciej Paszewski

Institute of Organic Chemistry, Polish Academy of Sciences, ul. Kasprzaka 44, 01-224 Warszawa 42, POB 58, Poland
Fax +48(22)6326681; E-mail: icho-s@icho.edu.pl

Received 30 April 2002; revised 10 July 2002

Abstract: A simple method of the synthesis of substituted nitrooxindoles via intramolecular oxidative nucleophilic substitution of hydrogen is described.

Key words: nucleophilic aromatic substitution, oxindoles, nitroacylanilides

The indole ring system is present in many natural products, pharmaceuticals, agrochemicals, etc. Thus, there is a continuous quest for efficient methods of synthesis of indole derivatives.[1] Of great interest are also methods of synthesis of oxindoles.[2] Amongst numerous methods applicable for construction of the indole ring, we are particularly interested in those based on nucleophilic substitution of hydrogen in nitroarenes.[3] These methods use two principal approaches. One of them consists in the introduction of substituents *ortho* to the nitro group via vicarious nucleophilic substitution (VNS) or oxidative nucleophilic substitution of hydrogen (ONSH). After further transformations of the products, including reduction of the nitro group, the indole ring is formed.[4,5] Alternative approach use *m*-nitroaniline as the basic starting material, its further transformations including the key process of nucleophilic substitution of hydrogen with proper carbanions, leads to nitroindoles in which the nitrogen atom of the amino groups is found in the indole ring.[6] Perhaps the most attractive variant of the latter approach is the recently reported synthesis of nitroindoles via direct condensation of *m*-nitroaniline with enolates of ketones.[7] Nitrooxindoles were prepared via intramolecular VNS reaction of *m*-nitroanilides of α-halocarboxylic acids.[8]

In this paper, we report that nitrooxindoles can be readily obtained from simpler starting materials, *m*-nitroanilides of carboxylic acids via intramolecular ONSH reaction. The reaction consists in the treatment of *m*-nitroanilides of alkanoic acids with a strong base, which abstracts a proton from the acyl moiety. The generated carbanions add intramolecularly to the nitroaromatic ring *ortho/para* to the nitro group giving anionic σ^H adducts that are subsequently oxidized to form the oxindole ring. Since acidity of NH hydrogen of the *m*-nitroanilides is similar or even higher than that of α-methyl or α-methylenic protons of the acyl moieties, for the reaction to proceed the NH proton should be replaced by a substituent, for instance, a methyl group. Thus, *N*-methyl *m*-nitroacylanilides were used in our studies. Amongst a few base-solvent systems typically used for generation of carbanions, *t*-BuOK/DMSO at room temperature was found to give the best results. It should be mentioned that formation of oxindoles via the intramolecular ONSH reaction of *m*-nitroacylanilides is accompanied with a deep blue or red coloration of the reaction mixture because highly colored *o*- and *p*-nitrobenzylic carbanions are produced. The process and results are presented in Scheme 1 and Table 1.

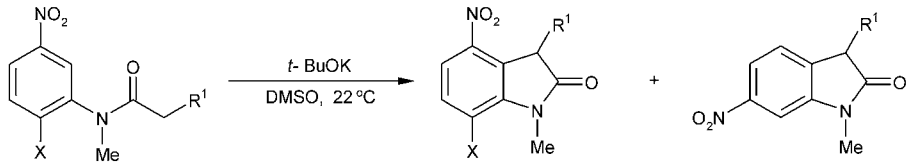
Intramolecular substitutions of hydrogen in the nitroaryl ring, which proceeds in the vicinity of the amide moiety, can take place in two positions: *ortho* and *para* in relation to the nitro group giving two isomeric 4- and 6-nitrooxindoles **2** and **3**, respectively. In all cases of the *m*-nitroacylanilides studied there was strong preference for the reaction to occur in the more sterically hindered position *ortho* to the nitro group to give 4-nitrooxindoles **2** as the main products. Tendency for such orientation was already observed in inter- and intramolecular VNS reactions [9] and also in the synthesis of nitroindoles via the reaction of ketones with *m*-nitroaniline.[7] The intramolecular reaction of carbanions generated from 6-chloro-3-nitroacylanilides can proceed via ONSH at position 2 to produce 7-chloro-4-nitrooxindoles or by conventional nucleophilic substitution of the halogen (S_NAr) to give 6-nitrooxindoles. Although in the reaction of anilides **1e**–**h** two nitrooxindoles are formed: expected 7-chloro-4-nitrooxindoles and products which do not contain the halogen, the latter were identical to the main products obtained from anilides **1a**–**d**, thus were obviously produced not via intramolecular S_NAr of the halogen but via dehalogenation proceeding during the reaction. A similar dehalogenation process was observed in the synthesis of indoles via direct condensation of enolates with 2-chloro-5-nitroaniline.[7]

This observation provides additional support to the general rule that nucleophilic addition of carbanions to nitroaromatic rings proceeds usually faster in positions occupied with hydrogen than in those, similarly activated, occupied with halogens.[10]

It appears that the anionic σ^H adducts produced via intramolecular addition of the carbanion of nitroacylanilides are oxidized by air oxygen always present in the system. When the reaction of **1b** was carried out in meticulously deoxygenated system, the oxindole was not

Synthesis 2002, No. 15, Print: 29 10 2002.
Art Id.1437-210X,E;2002,0,15,2203,2206,ftx,en;Z06902SS.pdf.

ISSN 0039-7881



1a-h **2a-h** **3a-d**

X = H, R^1 = H, **a**; Me, **b**; Et, **c**; Ph, **d**.
X = Cl, R^1 = H, **e**; Me, **f**; Et, **g**; Ph, **h**.

Scheme 1

formed; on the other hand bubbling of oxygen in the reaction mixture does not change the results.

Table 1 Substituted Nitrooxindoles **2** (and **3**) Prepared

Entry	X	R^1	No	Products, Yield (%)		
1[a]	H	H	**1a**	**2a**, 35	–	**3a**, traces
2	H	Me	**1b**	**2b**, 64	–	**3b**, traces
3	H	Et	**1c**	**2c**, 56	–	**3c**, 9
4	H	Ph	**1d**	**2d**, 45	–	**3d**, 12
5[a]	Cl	H	**1e**	**2e**, 29	–	–
6	Cl	Me	**1f**	**2f**, 33	**2b**, 17	–
7	Cl	Et	**1g**	**2g**, 38	**2c**, 23	–
8	Cl	Ph	**1h**	**2h**, 32	**2d**, 27	–

[a] Three equivalents of *t*-BuOK were used.

Commercial DMSO and DMF were distilled over CaH_2 and stored over molecular sieves. Column chromatography was performed using Merck Kieselgel 60. ^{1}H NMR and ^{13}C NMR were recorded on Varian Gemini (200 MHz) and Varian Mercurry (400 MHz) spectrometers. Chemical shifts (δ) are given in ppm downfield from TMS. Coupling constants are given in Hz. MS were measured on AMD 604 spectrometer.

Starting materials: 3′-nitroacetanilide,[11] 2′-chloro-5′-nitroacetanilide,[11] *N*-methyl-3′-nitroacetanilide (**1a**),[12] *N*-methyl-3-nitroaniline[12] and *N*-Methyl-2′-chloro-5′-nitroacetanilide (**1e**)[12] were prepared according to reported procedures. Compounds **1b**–**d** were prepared via acylation of *N*-methyl-3-nitroaniline with appropriate acyl chlorides, whereas **1f**–**h** were prepared via methylation of appropriate 2′-chloro-5′-nitroacylanilides.

It was observed that in ^{1}H and ^{13}C NMR spectra of compounds **1a**–**h** some signals were broadened or doubled. This is caused by restricted internal rotation of N–C(O) bond and is often observed in the NMR spectra of amides.[13]

***N*-Methyl-3′-nitropropionanilide (1b); Typical Procedure**
To a solution of *N*-methyl-3-nitroaniline (4.26 g, 28 mmol) in anhyd toluene (60 mL) were added a solution of propionyl chloride (2.98 g, 32 mmol) in toluene (5 mL) and Et_3N (3.4 g, 33.6 mmol). The mixture was stirred for 3 h at r.t. and treated with H_2O (150 mL) and EtOAc (100 mL). The organic layer was separated washed and dried. The solvents were evaporated and the residue recrystallized from hexane–toluene to give **1b**; yield: 4.95 g (85)%; mp 64 °C.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.11 (t, 3 H, *J* = 7.4 Hz), 2.16 (br, 2 H), 3.34 (s, 3 H), 7.55–7.68 (m, 2 H), 8.08–8.12 (m, 1 H), 8.17–8.24 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 9.41, 27.70, 37.37, 122.21, 130.41, 133.32, 145.24, 148.89, 173.40.

MS (EI): *m*/*z* (%) = 208 (M^+, 14), 152 (100), 106 (14), 57 (32).

Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.69; H, 5.81; N, 13.45. Found: C, 57.33; H, 6.05; N, 13.27.

***N*-Methyl-3′-nitrobutyranilide (1c)**
Yield: 87%; mp 51°C (hexane–toluene).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (br, 3 H), 1.45 (m, 2 H), 2.1 (br, 2 H), 3.34 (s, 3 H), 7.56–7.66 (m, 2 H), 8.09 (m, 1 H), 8.20 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 13.75, 18.66, 36.15, 37.37, 122.33, 130.47, 133.44, 145.28, 148.88, 172.61.

MS (EI): *m*/*z* (%) = 222 (M^+, 13), 152 (100), 106 (16), 71 (42), 43 (61).

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.6. Found: C, 59.42; H, 6.54; N, 12.65.

***N*-Methyl-(3′-nitro)phenylacetanilide (1d)**
Yield: 75%; mp 70–72 °C (hexane–toluene).

^{1}H NMR (400 MHz, acetone-d_6): δ = 3.32 (br, 3 H), 3.58 (br, 2 H), 7.1 (br, 1 H), 7.16–7.26 (m, 2 H), 7.7–7.78 (m, 3 H), 8.12 (br, 1 H), 8.21 (br, 1 H).

^{13}C NMR ($CDCl_3$): δ = 37.61, 41.67, 96.6, 127.25, 128.99, 131.39, 136.39, 146.21, 149.62.

MS (EI): *m*/*z* (%) = 270 (M^+, 22), 152 (50), 118 (36), 91 (100).

Anal. Calcd for $C_{15}H_{14}N_2O_3$: C, 66.66; H, 5.22; N, 10.36. Found: C, 66.6; H, 5.17; N, 10.25.

(2′-Chloro-5′-nitro)acetanilide
Yield: 86%; mp 160 °C (EtOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.28 (s, 3 H), 7.51 (d, 1 H, *J* = 8.8 Hz), 7.65 (br s, 1 H), 7.86–7.92 (m, 1 H), 9.3 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 24.86, 96.1, 116.27, 118.97, 128.37, 129.49, 135.47, 147.17, 168.33.

MS (EI): *m*/*z* (%) = 214 (M^+, 18), 179 (25), 172 (100), 126 (20), 90 (17), 43 (79).

Anal. Calcd for $C_8H_7ClN_2O_3$: C, 44.77; H, 3.29; Cl, 16.52; N, 13.05. Found: C, 44.76; H, 3.36; Cl, 16.69; N, 13.06.

(2′-Chloro-5′-nitro)propionanilide
Yield: 71%; mp 124–125 °C (hexane–toluene).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.3 (t, 3 H, *J* = 7.5 Hz), 2.54 (q, 2 H, *J* = 7.5 Hz), 7.54 (d, 1 H, *J* = 8.8 Hz), 7.77 (s, 1 H), 7.9 (dd, 1 H, *J* = 8.8, 2.7 Hz), 9.35 (d, 1 H, *J* = 2.7 Hz).

^{13}C NMR ($CDCl_3$): δ = 9.25, 30.91, 116.16, 118.77, 128.36, 129.43, 135.5, 147.19, 172.06.

MS (EI): *m*/*z* (%) = 228 (M^+, 25), 193 (23), 172 (59), 126 (17), 90 (22), 57 (100).

Anal. Calcd for $C_9H_9ClN_2O_3$: C, 47.28; H, 3.97; Cl, 15.51; N, 12,25. Found: C, 47.36; H, 4.11; Cl, 15.52; N, 12.18.

(2′-Chloro-5′-nitro)butyranilide
Yield: 67%; mp 129–130 °C (hexane–toluene).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.05 (t, 3 H, *J* = 7.3 Hz), 1.7–1.9 (m, 2 H), 2.48 (t, 2 H, *J* = 7.3 Hz), 7.54 (d, 1 H, *J* = 8.8 Hz), 7.75 (br, 1 H), 7.92 (dd, 1 H, *J* = 8.8, 2.6 Hz), 9.35 (d, 1 H, *J* = 2.6 Hz).

^{13}C NMR ($CDCl_3$): δ = 13.62, 18.72, 39.68, 116.21, 118.79, 128.39, 129.43, 135.49, 147.11, 171.35.

MS (EI): *m*/*z* (%) = 242 (M^+, 13), 172 (73), 71 (60), 43 (100).

Anal. Calcd for $C_{10}H_{11}ClN_2O_3$: C, 49.58; H, 4.58; Cl, 14.45; N, 11.57. Found: C, 49.36; H, 4.72; Cl, 14.37; N, 11.48.

(2′-Chloro-5′-nitro)phenylacetanilide
Yield: 65%; mp 188–190°C (EtOH–H_2O).

^{1}H NMR (400 MHz, acetone-d_6): δ = 3.93 (s, 2 H), 7.27–7.34 (m, 1 H), 7.35–7.42 (m, 2 H), 7.42–7.5 (m, 2 H), 7.73 (d, 1 H, *J* = 8.7 Hz), 7.98 (dd, 1 H, *J* = 2.8, 8.7 Hz), 8.91 (br, 1 H), 9.21 (d, 1 H, *J* = 2.8 Hz).

^{13}C NMR (acetone-d_6): δ = 44.39, 96.61, 117.63, 120.0, 127.93, 129.49, 130.3, 131.02, 135.83, 137.02, 170.64

MS (EI): *m*/*z* (%) = 290 (M^+, 10), 255 (14), 118 (89), 91 (100), 65 (10).

Anal. Calcd for $C_{14}H_{11}ClN_2O_3$: C, 57.84; H, 3.81; Cl, 12.2; N, 9.64. Found: C, 57.69; H, 3.73; Cl, 12.32; N, 9.43.

Methylation of 2′-Chloro-5′-nitroacylanilides; *N*-Methyl-(2′-chloro-5′-nitro)propionanilide (1f); Typical Procedure
To a solution of (2′-chloro-5′-nitro)propionanilide (3.63 g, 15 mmol) in anhyd DMF (50 mL) under argon at r.t. was added *t*-BuOK (2.02 g, 18 mmol). After 5 min, to the dark red solution was added MeI (2.8 mL, 45 mmol) and the mixture was stirred for 1 h. The mixture was treated with dil. HCl (150 mL) and extracted with EtOAc. The extracts were washed, dried ($MgSO_4$) and the solvent evaporated. The residue was recrystallized from hexane–toluene to give **1f**; yield: 85%; mp 54 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09 (t, 3 H, *J* = 7.4 Hz), 1.94–2.05 (m, 2 H), 3.24 (s, 3 H), 7.73 (d, 1 H, *J* = 8.7 Hz), 8.19–8.24 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 9.22, 27.40, 35.74, 124.20, 125.19, 131.52, 140.65, 142.33, 147.27, 173.10.

MS (EI): *m*/*z* (%) = 242 (M^+, 2), 213 (25), 207 (79), 186 (85), 57 (100).

Anal. Calcd for $C_{10}H_{11}ClN_2O_3$: C, 49.5; H, 4.57; Cl, 14.61; N, 11.54. Found: C, 49.61; H, 4.71; Cl, 14.73; N, 11.48.

***N*-Methyl-(2′-chloro-5′-nitro)acetanilide (1e)**
Yield: 70%; mp 105–107 °C (EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84 and 2.32 (2 s, 3 H each), 3.24 and 3.38 (2 s, 3 H each), 7.74 (m, 1 H), 8.21–8.24 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 21.65, 21.92, 35.69, 38.36, 96.10, 123.49, 124.22, 125.07, 131.02, 131.50, 140.47, 142.71, 147.31, 169.51.

MS (EI): *m*/*z* (%) = 228 (M^+,4), 213 (9), 193 (92), 186 (66), 140 (33), 104 (14), 77 (20), 43 (100).

Anal. Calcd for $C_{10}H_{11}ClN_2O_3$: C, 49.5; H, 4.57; Cl, 14.61; N, 11.54. Found: C, 49.61; H, 4.71; Cl, 14.72; N, 11.48.

***N*-Methyl-(2′-chloro-5′-nitro)butyranilide (1g)**
Yield: 90%; mp 46–47 °C (heptane).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.85 (t, 3 H, *J* = 7.3 Hz), 1.56–1.72 (m, 2 H), 1.90–2.00 (m, 2 H), 3.23 (s, 3 H), 7.74 (d, 1 H, *J* = 8.6 Hz), 8.18–8.24 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 13.69, 18.34, 35.66, 35.85, 124.17, 125.19, 131.5, 140.60, 142.36, 147.18, 172.25.

MS (EI): *m*/*z* (%) = 221 (M^+, 69), 188 (32), 186 (100), 140 (12), 71 (81), 43 (99), 41 (19).

Anal. Calcd for $C_{11}H_{13}ClN_2O_3$: C, 51.47; H, 5.1; Cl, 13.81; N, 10.91. Found: C, 51.23; H, 5.26; Cl, 13.98; N, 10.77.

***N*-Methyl-(2′-Chloro-5′-nitro)phenylacetanilide (1h)**
Yield: 88%; mp 164 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.24 (s, 3 H), 3.33 (d, 1 H, *J* = 15 Hz), 3.51 (d, 1 H, *J* = 15 Hz), 6.92–6.96 (m, 2 H), 7.18–7.23 (m, 3 H), 7.68 (d, 1 H, *J* = 8.8 Hz), 7.89 (d, 1 H, *J* = 2.7 Hz), 8.18 (dd, 1 H, *J* = 8.8, 2.7 Hz).

^{13}C NMR ($CDCl_3$): δ = 36.10, 41.72, 124.22, 125.80, 127.04, 128.51, 128.71, 131.32, 134.05, 140.64, 141.83, 146.86, 170.36.

MS (EI): *m*/*z* (%) = 304 (M^+, 4), 269 (54), 213 (12), 186 (19), 118 (45), 91 (100).

Anal. Calcd for $C_{15}H_{13}ClN_2O_3$: C, 59.12; H, 4.3; Cl, 11.63; N, 9.19. Found: C, 58.92; H, 4.23; Cl, 11.55; N, 8.98.

1,3-Dimethyl-4-nitrooxindole (2b); Typical Procedure
To a stirred solution of *t*-BuOK (170 mg, 1.5 mmol) in anhyd DMSO (10 mL) was added dropwise a solution of **1b** (208 mg, 1 mmol) in DMSO (5 mL) during 20 min at r.t. The dark blue mixture was stirred for 40 min, treated with dil. HCl (100 mL) and extracted with EtOAc. The combined organic extracts were washed, dried, the solvent evaporated and the residue purified by column chromatography on silica gel using hexane–EtOAc as eluent to give **2b**; yield: 64%; mp 148–150 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (d, 3 H, *J* = 7.5 Hz), 3.27 (s, 1 H), 4.03 (q, 1 H, *J* = 7.5 Hz), 7.12 (d, 1 H, *J* = 7.8 Hz), 7.47 (m, 1 H), 7.82 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 14.9, 26.64, 41.83, 113.07, 117.38, 126.67, 129.07, 144.94, 146.32, 177.74,

MS (EI): *m*/*z* (%) = 206 (M^+, 100), 189 (17), 160 (35), 117 (38).

Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.03; H, 5.09; N, 13.37.

1-Methyl-4-nitrooxindole (2a)
Yield: 35%; mp 149–151 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.28 (s, 3 H), 4.00 (s, 2 H), 7.12 (d, 1 H, *J* = 7.7 Hz), 7.49 (m, 1 H), 7.87 (dd, 1 H, *J* = 9.6, 0.8 Hz).

^{13}C NMR ($CDCl_3$): δ = 26.61, 37.02, 113.10, 117.03, 121.25, 129.16, 144.31, 147.24, 173.85.

MS (EI): *m*/*z* (%) = 192 (M^+,100), 175 (35), 147 (38), 117 (31), 91 (28).

Anal. Calcd for $C_9H_8N_2O_3$: C, 56.25; H, 4.2; N, 14.58. Found: C, 56.02; H, 4.26; N, 14.41.

3-Ethyl-1-methyl-4-nitrooxindole (2c)
Yield: 56%; mp 114–115 °C (hexane–EtOAc).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.67 (t, 3 H, *J* = 7.5 Hz), 2.05–2.25 (m, 2 H), 3.27 (s, 3 H), 4.11 (m, 1 H), 7.10 (d, 1 H, *J* = 7.7 Hz), 7.47 (m, 1 H), 7.82 (dd, 1 H, *J* = 0.9, 8.5 Hz).

^{13}C NMR ($CDCl_3$): δ = 9.23, 22.45, 26.49, 47.55, 112.75, 117.37, 124.81, 129.08, 145.11, 146.99, 177.03.

MS (EI): *m*/*z* (%) = 220 (M^+, 32), 192 (100), 161 (14), 146 (17), 133 (12).

3-Ethyl-1-methyl-6-nitrooxindole (3c)
Yield: 9%; mp 117 °C (hexane–EtOAc).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.9 (t, 3 H, *J* = 7.5 Hz), 2.05–2.11 (m, 2 H), 3.29 (s, 3 H), 3.52 (m, 1 H), 7.39 (m, 1 H), 7.65 (d, 1 H, *J* = 2.1 Hz), 7.98 (dd, 1 H, *J* = 2.1, 8.1 Hz).

^{13}C NMR ($CDCl_3$): δ = 9.99, 23.5, 26.44, 46.64, 102.73, 117.95, 123.98, 136.2, 145.73, 148.28, 177.03

MS (EI): *m*/*z* (%) = 220 (M^+, 29), 192 (100), 161 (12), 146 (19).

Anal. Calcd for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 59.84; H, 5.41; N, 12.55.

1-Methyl-4-nitro-3-phenyloxindole (2d)
Yield: 45%; mp 168 °C (hexane–EtOAc).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.29 (s, 3 H), 5.14 (s, 1 H), 7.08 (m, 2 H), 7.2 (d, 1 H, *J* = 7.8 Hz), 7.22–7.30 (m, 3 H), 7.56 (m, 1 H), 7.85 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.97, 53.12, 96.60, 114.65, 117.75, 125.46, 128.22, 128.63, 129.41, 130.93, 136.55, 145.63, 148.46, 175.17.

MS (EI): *m*/*z* (%) = 268 (M^+, 100), 251 (24), 234 (65), 165 (25).

Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.01; H, 4.37; N, 10.27.

1-Methyl-6-nitro-3-phenyloxindole (3d)
Yield: 12%; mp 169–71 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (s, 3 H), 4.69 (s, 1 H), 7.13–7.2 (m, 2 H), 7.26–7.38 (m, 4 H), 7.74 (d, 1 H, *J* = 2.1 Hz), 7.99 (dd, 1 H, *J* = 2.1, 8.1 Hz).

^{13}C NMR ($CDCl_3$): δ = 26.81, 51.88, 103.08, 118.31, 125.37, 128.13, 128.31, 129.16, 134.92, 135.85, 145.60, 148.58, 175.25.

MS (EI): *m*/*z* (%) = 268 (M^+, 100), 251 (20), 239 (12), 222 (30), 193 (26).

Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 66.69; H, 4.25; N, 10.00.

7-Chloro-1-methyl-4-nitrooxindole (2e)
Yield: 29%; mp 165 °C (hexane–EtOAc).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.64 (s, 3 H), 4.03 (s, 2 H), 7.41 (d, 1 H, *J* = 9.0 Hz), 7.79 (d, 1 H, *J* = 9.0 Hz).

^{13}C NMR ($CDCl_3$): δ = 29.62, 37.00, 96.10, 117.77, 121.11, 123.86, 131.37, 142.86, 173.83.

MS (EI): *m*/*z* (%) = 226 (M^+, 100), 209 (30), 181 (29), 179 (12), 151 (14), 117 (35).

Anal. Calcd for $C_9H_7ClN_2O_3$: C, 47.7; H, 3.11; Cl, 15.64; N, 12.36. Found: C, 47.81; H, 3.24; Cl, 15.30; N, 12.29.

7-Chloro-1,3-dimethyl-4-nitrooxindole (2f)
Yield: 33%; mp 124–125 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, 3 H, *J* = 7.5 Hz), 3.67 (s, 3 H), 4.07 (q, 1 H, *J* = 7.5 Hz), 7.38 (dd, 1 H, *J* = 9.1, 0.6 Hz), 7.73 (d, 1 H, *J* = 9.1 Hz).

^{13}C NMR ($CDCl_3$): δ = 15.28, 29.73, 41.53, 118.13, 121.04, 129.38, 131.27, 141.98, 143.52, 177.88.

MS (EI): *m*/*z* (%) = 240 (M^+, 100), 223 (72), 208 (21), 195 (44), 166 (12), 131 (22).

Anal. Calcd for $C_{10}H_9ClN_2O_3$: C, 49.91; H, 3.77; Cl, 14.73; N, 11.64. Found: C, 49.82; H, 3.83; Cl, 14.57; N, 11.8.

7-Chloro-3-ethyl-1-methyl-4-nitrooxindole (2g)
Yield: 38%; mp 115 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.7 (t, 3 H, *J* = 7.6 Hz), 2.0–2.1 (m, 1 H), 2.1–2.2 (m, 1 H), 3.63 (s, 3 H), 4.8 (m, 1 H), 7.39 (dd, 1 H, *J* = 9.1, 0.7 Hz), 7.72 (d, 1 H, *J* = 9.1 Hz).

^{13}C NMR ($CDCl_3$): δ = 9.28, 22.96, 29.55, 47.19, 118.09, 120.79, 127.63, 131.29, 142.56, 143.62, 177.18.

MS (EI): *m*/*z* (%) = 254 (M^+, 33), 228 (32), 226 (100), 220 (13), 196 (17), 180 (15).

Anal. Calcd for $C_{11}H_{12}ClN_2O_3$: C, 51.88: H, 4.35; Cl, 13.92; N, 11.00. Found: C, 51.72; H, 4.46; Cl, 13.71; N, 11.04.

7-Chloro-1-methyl-4-nitro-3-phenyloxindole (2h)
Yield: 32%; mp 165–166 °C (hexane–EtOAc).

^{1}H NMR (400 MHz, acetone-d_6): δ = 3.61 (s, 3 H), 5.22 (s, 1 H), 7.11–7.15 (m, 2 H), 7.24–7.31 (m, 3 H), 7.66 (dd, 1 H, *J* = 9.0, 0.7 Hz), 7.79 (d, 1 H, *J* = 9.0 Hz).

^{13}C NMR (acetone-d_6): δ = 52.84, 96.61, 118.90, 121.38, 128.41, 128.44, 128.69, 129.52, 132.87, 136.08, 144.05, 144.5, 175.52.

MS (EI): *m*/*z* (%) = 302 (M^+, 100), 285 (28), 268 (65).

HRMS: *m*/*z* calcd for $C_{15}H_{11}ClN_2O_3$: 302.04582; found: 302.04849.

Acknowledgement

This work was supported by State Committee for Scientific Research Grant No. PBZ 6.01.

References

(1) (a) Sundberg, R. J. *Indoles*; Academic Press: San Diego, **1996**. (b) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045.
(2) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402.
(3) (a) Mąkosza, M.; Wojciechowski, K. *Heterocycles* **2001**, *54*, 445. (b) Mąkosza, M. *Pure Appl. Chem.* **1997**, *69*, 559.
(4) (a) Wojciechowski, K.; Mąkosza, M. *Bull. Chim. Soc. Belg.* **1986**, *95*, 671. (b) Wojciechowski, K.; Mąkosza, M. *Synthesis* **1986**, 651.
(5) Mąkosza, M.; Danikiewicz, W.; Wojciechowski, K. *Liebigs Ann. Chem.* **1988**, 203.
(6) Wojciechowski, K.; Mąkosza, M. *Tetrahedron Lett.* **1984**, *25*, 4793.
(7) Moskalev, N.; Mąkosza, M. *Tetrahedron Lett.* **1999**, *40*, 5395.
(8) Mąkosza, M.; Hoser, H. *Heterocycles* **1994**, *37*, 1701.
(9) Mąkosza, M.; Glinka, T.; Kinowski, J. *Tetrahedron* **1984**, *40*, 1863.
(10) (a) Mąkosza, M. *Russ. Chem. Bull.* **1996**, *45*, 491. (b) Terrier, F. *Nucleophilic Aromatic Displacement*; VCH: New York, **1991**. (c) Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; Academic Press: San Diego, **1999**.
(11) Rosevear, J.; Wilshire, J. F. K. *Aust. J. Chem.* **1985**, *38*, 723.
(12) Svoboda, P.; Pytela, O.; Vecera, M. *Collect. Czech. Chem. Commun.* **1987**, *52*, 2217.
(13) Curray, D. P.; Yu, H.; Liu, H. *Tetrahedron* **1994**, *50*, 7343.