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Dill and parsley seed extracts in scale up synthesis of aminopolyalkoxybenzenes - beneficial synthons for fused nitrogen polyalkoxyheterocycles

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Experimental

NMR spectra were collected on a Bruker DR-500 instrument [working frequencies of 500.13 MHz (^{1}H) and 75.47 (^{13}C)]. Mass spectra were obtained on a Finnigan MAT/INCOS 50 instrument (70 eV) using direct probe injection. Elemental analysis was accomplished with the automated Perkin-Elmer 2400 CHN microanalyzer. Melting points were measured on a «Boetius» bench. The purity of targeted products were monitored by thin layer chromatography on the «Merck 60F_{254}» plates.

Liquid phase hydrogenation was carried out in stainless still reactor partially filled with block highly porous cellular catalyst [1], commercially available at www.rus-cat.com and www.chemblock.com. Highly porous ceramic material (α-Al_2O_3) covered by sol γ-Al_2O_3 with pores no less than 70–95% was used as catalyst carrier, readily permeable to air and water. This catalyst carrier was impregnated with $Pd(NO_3)_2$ and heated at 450 °C to afford PdO-coating catalyst. PdO was hydrogenated to metallic Pd by hydrogen at 50–55 °C, yielding the targeted block highly porous ceramic catalyst with 1% Pd/6% γ-Al_2O_3. This type of block catalysts can be repeatedly regenerated by heating at 400-450 °C up to 30–40 times without activity loss.

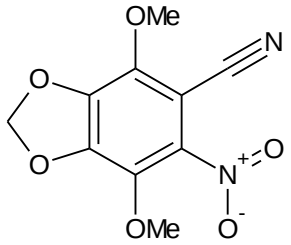
Recently, the preparation technology of different size blocks was reported [2,3,4]. Block highly porous ceramic catalyst cylinder (1% Pd/6% γ-Al_2O_3, 50 mm diameter, 50 mm height, 10 ppi cell, 33.9 g, 70–95% pores) was fixed in the middle of stainless steel cylinder autoclave (50 mm inner diameter) equipped with thermocouple, hydrogen inlet tube, and electric heating system. The stirring of the reaction mixture was provided by shaking device (capacity 120–160 shaking/min).

General Experimental Procedures. Chemistry.

Parsley and dill seed essential oils containing apiol (**1a**) and dillapiol (**1b**) were obtained -by liquid CO_2 extraction at Company Karawan Ltd. (Krasnodar, Russia, http://kuban-karawan.ru/). For the extraction, parsley and dill varieties with the highest content of **1a** and **1b** were chosen. The essential oil of cultivated in Russia parsley var. *Sakharnaya* contained 70–75% of **1a**. Indian dill seeds essential oil contained 30–33% of **1b** [5] .

Apiol (**1a**) and dillapiol (**1b**) with 98–99% purity on a kg-scale were obtained by high-efficiency distillation using a pilot plant device at N.D. Zelinsky Institute of Organic Chemistry RAS (Moscow, Russia). Propenylbenzenes **2a,b** were prepared from **1a,b** according to a published procedure. [6]. Ozonolysis of **2a** and **2b** was conducted using a custom-designed apparatus (Science and Technology Park, St. Petersburg State Polytechnic University, Russia) equipped with an IR ozone detector (Japan) and an automated shut-down circuit. The device allowed for the controlled generation of ozone from O_2, with a maximal capacity of 10 g of O_3 per hour.

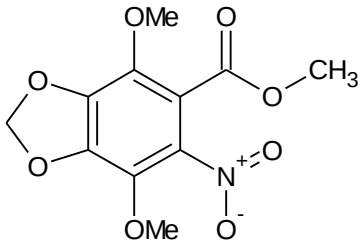
2,5-Dimethoxy-3,4-methylenedioxy-6-nitrobenzonitrile (7a)



HNO_3 (98%, 8 mL, 192 mmol) was added dropwise on stirring to the solution of apiolbenzonitrile **4a** [6] (10g, 48 mmol) in dry $CHCl_3$ (100 mL), maintaining the temperature of 0 °C. The reaction mixture was stirred at 0 °C for 1 h, diluted with ice-water (100 g), and stirred for additional 2 h at room temperature. The $CHCl_3$-phase was washed with water (50 mL), aqueous solution of $NaHCO_3$ (10%, 50 mL), again by water (50 mL), and evaporated *in vacuo*. The residue was crystallized from EtOH to afford **7a.**

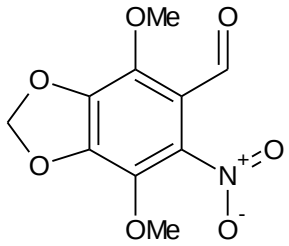
Yield 11.75 g (97%), yellow powder, mp 138–140 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ6.36 (2H, s, OCH_2O), 4.08 (3H, s, OCH_3), 3.96 (3H, s, OCH_3). EIMS *m*/*z* 252 $[M]^+$ (100), 237 (10), 222 (10), 191(69), 164 (20), 146 (15), 131 (34), 120 (25), 118 (31), 107 (13), 105 (19 (37), 103 (40), 102 (34), 90 (81), 83 (26), 78 (77), 75 (59), 64 (27), 62 (41). Anal. C 47.63, H 3.20, N 11.11%, calcd for $C_{10}H_8N_2O_6$, C 47.71, H 3.24, N 11.02%.

2,5-Dimethoxy-3,4-methylenedioxy-6-nitrobenzoic acid methyl ester (8a)



HNO_3 (98%, 4 mL, 96 mmol) was added dropwise on stirring to the solution of apiolic acid methyl ester **6a** [6] (5g, 21 mmol) in dry $CHCl_3$ (50 mL), maintaining the temperature of 0 °C. The reaction mixture was stirred at 0 °C for 40 min and diluted with ice-water (100 g). The $CHCl_3$ phase was separated and the water phase was extracted with $CHCl_3$ (2 × 40 mL). The combined $CHCl_3$ phases were washed with water (40 mL), aqueous solution of $NaHCO_3$ (10%, 40 mL), again with water (40 mL), and evaporated *in vacuo*. The residue was crystallized from MeOH to afford **8a.** Yield 5.54 g (93%), cream powder, mp 100–101 °C (lit.[7] 102.5 °C). ^{1}H NMR (DMSO-d_6, 500 MHz):: δ 6.29 (2H, s, OCH_2O), 3.95 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 3.77 (3H, s, OCH_3). EIMS *m*/*z* 285 $[M]^+$ (100), 254 (52), 239 (17), 238 (21), 209 (61), 180 (22), 121 (13), 120 (13), 107 (11), 95 (19), 92 (22), 82 (42), 77 (21), 69 (25), 59 (27). Anal. C 49.63, H 3.79, N 10.52 %, calcd for $C_{11}H_{11}NO_8$, C 49, H 3, N 10 %.

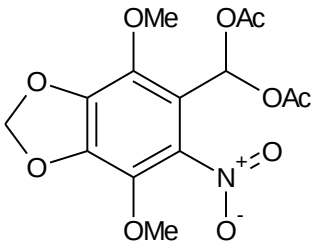
2,5-Dimethoxy-3,4-methylenedioxy-6-nitrobenzaldehyde (9a)



HNO_3 (62%, 18 mL, 244 mmol) was added dropwise on stirring to the solution of apiol aldehyde **3a** (20g, 95 mmol) in AcOH (80 mL) and Ac_2O (20 mL), maintaining the temperature of 30–40 °C. The reaction mixture was cooled to room temperature, stored for 30 min, and diluted with ice-water (200 g). The residue was filtered, washed by water, and dried in air to afford 22.2 g of mixture of 6-nitrobenzaldehyde **9a**, diacetate **11a**, and 2,5-dimethoxy-3,4-methylenedioxy-1-nitrobenzene **12a**[8] in ratio 25:1:2 (NMR/18277590). Final crystallization from EtOH afforded target **9a.** Yield 18.4 g (76 %), yellow powder, mp 135–137 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.05 (1H, s, CHO), 6.33 (2H, s, OCH_2O), 4.05 (3H, s, OCH_3), 3.92 (3H, s, OCH_3). EIMS *m*/*z* 255 $[M]^+$ (12), 238 (7), 210 (14), 207 (11), 195 (37), 180 (16), 179 (16), 150 (12), 149 (11), 137 (10), 121 (10), 120 (14), 107

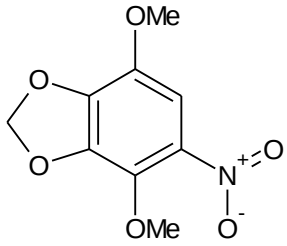
(30), 106 (19), 95 (28), 93 (42), 92 (43), 83 (38), 77 (68), 69 (41), 65 (62), 53 (100). Anal. C 47.07, H 3.55, N 5.49%, calcd for $C_{10}H_9NO_7$, C 47.15, H 3.58, N 5.42 %.

2,5-Dimethoxy-3,4-methylenedioxy-6-nitrobenzaldehyde diacetyl acylal (11a)



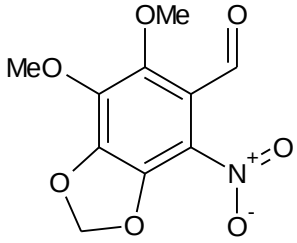
^{1}H NMR (DMSO-d_6, 500 MHz): δ7.74 (1H, s, CH), 6.25 (2H, s, OCH_2O), 4.05 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 2.05 (6H, s, $2C(O)CH_3$).

2,5-Dimethoxy-3,4-methylenedioxy-1-nitrobenze 12a



Yellow powder, mp 97–99 °C (lit. [9] 100 °C). ^{1}H NMR (DMSO-d_6, 500 MHz): δ7.31 (1H, s, CH), 6.22 (2H, s, OCH_2O), 3.92 (3H, s, OCH_3), 3.86 (3H, s, OCH_3). EIMS *m*/*z* 227 $[M]^+$ (100), 212 (10), 197 (7), 167 (25), 166 (25), 139 (26), 137 (17), 124 (17), 121 (15), 106 (25), 95 (26), 93 (27), 83 (18), 77 (32), 69 (23), 65 (58), 53 (66). Anal. C 47.58, H 3.99, N 6.17%, calcd for $C_9H_9NO_6$, C 47.65, H 4.02, N 6.12 %.

2,3-Dimethoxy-4,5-methylenedioxy-6-nitrobenzaldehyde (9b)



HNO_3 (98 %, 2.1 mL, 50 mmol) was added dropwise on stirring to the solution of dillapiolaldehyde **3b** (2.1 g, 10 mmol) in dry $CHCl_3$ (20 mL), maintaining the temperature of 0 °C. After addition of HNO_3 the reaction mixture was kept during 30 min at 0 °C and diluted with ice-water (50 g). Water phase was extracted with $CHCl_3$ (2 × 20 mL), combined with the initial $CHCl_3$ phase, and washed

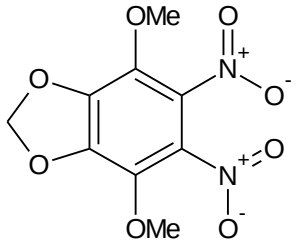
with water (30 mL), aqueous solution of $NaHCO_3$ (30 mL), and again with water (30 mL). The solution of $CHCl_3$ was dried in air and avaporated in vacuo to afford **9b.**

Yield 1.94 g (76 %), yellow powder, mp 162.5–164.5 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.07 (1H, s, CHO), 6.32 (2H, s, OCH_2O), 4.07 (3H, s, OCH_3), 3.87 (3H, s, OCH_3). EIMS *m*/*z* 255 $[M]^+$ (90), 238 (18), 225 (55), 210 (79), 207 (20), 195 (32), 180 (41), 179 (18), 167 (29), 150 (11), 149 (15), 137 (30), 121 (23), 120 (22), 107 (26), 106 (6), 95 (27), 93 (62), 92 (65), 83 (45), 77 (48), 69 (33), 65 (100), 53 (87). Anal. C 47.07, H 3.55, N 5.49%, calcd for $C_{10}H_9NO_7$, C 47.18, H 3.59, N 5.38 %.

General procedure for the nitration of tetralkoxybenzaldehydes (9a and 9b) to tetralkoxydinitrobenzenes (13a and 13b)

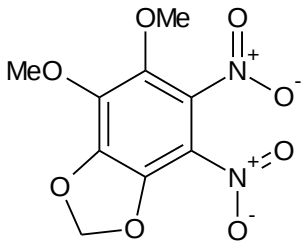
HNO_3 (72%, 190 mL, 3.1 mol) was added dropwise on stirring during 2 h to the solution of apiolaldehyde **3a** (40 g, 0.19 mol) in dry $CHCl_3$ (180 mL), maintaining the temperature of 0 °C. The reaction mixture was stirred for additional 3 h at 0 °C, 5 h at room temperature, and diluted with ice-water (400 g). Water phase was extracted with $CHCl_3$ (2 × 100 mL), combined with the initial $CHCl_3$ phase, and washed with water (100 mL), aqueous solution of $NaHCO_3$ (100 mL), and again with water (100 mL). Solution of $CHCl_3$ was dried in air and evaporated *in vacuo*. The residue was crystallized from EtOH to afford **13a.**

3,6-Dimethoxy-4,5-methylenedioxy-1,2-dinitrobenzene (13a)



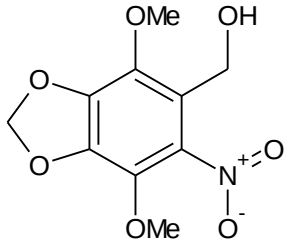
Yield 38.8 g (75 %), dark-yellow powder, mp 108–109.5 °C (lit. [10] 116 °C). ^{1}H NMR (DMSO-d_6, 500 MHz):: δ 6.20 (2H, s, OCH_2O), 4.04 (6H, s, $2OCH_3$). EIMS *m*/*z* 272 $[M]^+$ (37), 181 (14), 120 (41), 119 (12), 107 (37), 95 (28), 93 (30), 92 (100), 83 (86), 77 (29), 69 (65), 67 (41), 53 (37). Anal. C 39.72, H 2.96, N 10.29%, calcd for $C_9H_8N_2O_8$, C 39.66, H 2.92, N 10.38 %.

5,6-Dimethoxy-3,4-methylenedioxy-1,2-dinitrobenzene (13b)



Yield 5.1 g (79 %), dark-yellow powder, mp 99–101 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ6.39 (2H, s, OCH_2O), 4.15 (3H, s, OCH_3), 3.84 (3H, s, OCH_3). EIMS *m*/*z* 272 $[M]^+$ (100), 255 (6), 242 (3), 140(11), 123 (11), 120 (19), 107 (12), 92 (37), 83 (20), 80 (15), 77 (10), 64 (15). Anal. C 39.72, H 2.96, N 10.29%, calcd for $C_9H_8N_2O_8$, C 39.62, H 2.91, N 10.40 %.

2,5-Dimethoxy-3,4-methylenedioxy-6-nitrobenzyl alcohol (10a)



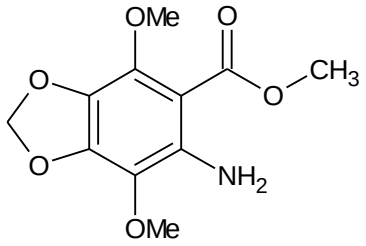
$NaBH_4$ (2.08 g, 55 mmol) was added to a warm solution (40 °C) of nitroapiolaldehyde **9a** (13g, 50.9 mmol) in the mixture of *i*-PrOH (260 mL) and MeOH (130 mL). The reaction mixture was stirred for 2 h at 40 °C, cooled to room temperature, mixed with AcOH (5 mL), evaporated to dryness, and diluted with water (150 mL). The deposit was filtered, washed with water (50 mL), and dried in air. Yield 12.4 g (95%), yellow powder, mp 54–55 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ6.17 (2H, s, OCH_2O), 5.10 (1H, s, OH), 4.42 (2H, d, J = 5.4 Hz, CH_2O), 3.90 (3H, s, OCH_3), 3.87 (3H, s, OCH_3). EIMS m/z 257 $[M]^+$ (70), 240 (18), 209 (10), 194 (15), 193 (19), 181 (18), 166 (24), 164 (23), 153 (18), 150 (23), 138 (21), 137 (20), 136 (26), 123 (33), 95 (57), 93 (50), 83 (81), 77 (67), 69 (82), 55 (77), 53 (100). Anal. C 49.63, H 3.79, N 10.52%, calcd for $C_{10}H_{11}NO_7$, C 49, H 3, N 10 %.

Hydrogenation of polyalkoxynitrobenzenes 7a, 8a, and 13a with block highly porous ceramic catalyst. General procedure A.

The solution of nitrobenzene (20 mmol) in MeOH (200 mL) in stainless steel autoclave filled with block highly porous ceramic catalyst cylinder (1% Pd/6% γ-Al_2O_3) was hydrogenated at room temperature during 3 h at pressure of 30 bar. The reaction mixture was removed from autoclave, the

solvent was evaporated, and the residue was recrystallized from a proper solvent to afford **15a** (or **16a**).

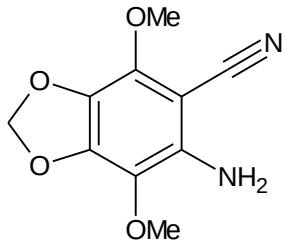
6-Amino-2,5-dimethoxy-3,4-methylenedioxybenzoic acid methyl ester (15a)



Yield 4.1 g (85 %), yellowish powder, mp 82-83 °C (lit.84.5 °C [11] 84.5 °C).

1H NMR (DMSO-d6, 500 MHz) 6.02 (2H, s, OCH_2O), 5.48 (2H, s, NH_2), 3.87 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.79 (3H, s, OCH_3). EIMS m/z 255 [M]+ (100). Anal. C 51.77, H 5.13, N 5.49%, calcd for C11H13NO6, C 51.72, H 5.10, N 5.54 %.

6-Amino-2,5-dimethoxy-3,4-methylenedioxybenzonitrile (16a)



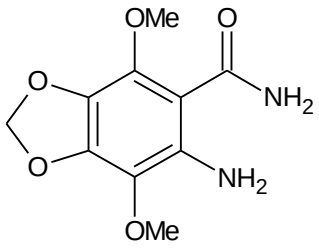
Yield 10 g (81%), yellow-green crystals, mp 118-120°C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ5.98 (2H, s, OCH_2O), 5.50 (2H, s, NH_2), 3.94 (3H, s, OCH_3), 3.75 (3H, s, OCH_3). EIMS *m*/*z* 222 $[M]^+$ (82), 207 (100), 179(10), 149 (23), 134 (13), 121 (15), 110 (17), 106 (12), 93 (15), 91 (21), 82 (42), 81 (35), 78 (33), 77 (29), 68 (37), 66 (68). Anal. C 54.05, H 4.54, N 12.61%, calcd for $C_{10}H_{10}N_2O_4$, C 54.11, H 4.57, N 12.55 %.

Hydrogenation of 6-nitro-2,5-dimethoxy-3,4-methylenedioxybenzonitrile (7a). General procedure B with conventional 5%Pd/C catalyst.

6-Amino-2,5-dimethoxy-3,4-methylenedioxybenzonitrile (16a)

Warm solution of 6-nitro-2,5-dimethoxy-3,4-methylenedioxybenzonitrile **7a** (14g, 55.5 mmol) in MeOH (650 mL) and granulated 5% Pd/C were placed into a standard stainless steel autoclave and hydrogenated at 40–45 °C during 4.5 h at pressure of 30 bar. Warm reaction mixture was removed from autoclave, the solvent was evaporated, and the residue was recrystallized from EtOH to afford **16a** as yellow-green crystals. Yield 9 g (73%), mp 118–120 °C.

6-Amino-2,5-dimethoxy-3,4-methylenedioxybenzamide 17a



Apart from nitrile **16a**, carboxamide **17a** was separated from EtOH solution as an additional hydrogenation product.

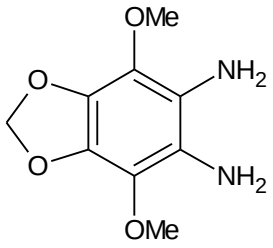
Yield 1.23 g (10%), yellowish power, mp 162–163 °C (EtOH).

^{1}H NMR (DMSO-d_6, 500 MHz): □ 7.44 and 7.23 (2s, 2H, C(O)NH_2), 6.09 (2H, s, NH_2), 5.92 (2H, s, OCH_2O), 6.09 (2H, s, NH_2), 3.86 (3H, s, OCH_3), 3.77 (3H, s, OCH_3). EIMS *m*/*z* 240 $[M]^+$ (100), 223 (65), 222 (60), 209 (22), 208 (91), 194 (65), 193 (21), 178(19), 171 (16), 150 (19), 111 (18), 110 (15), 94 (20), 93 (17), 92 (18), 83 (62), 82 (44), 81 (17), 69 (50), 68 (79), 67 (31). Anal. C 50.00, H 5.04, N 11.66%, calcd for $C_{10}H_{12}N_2O_5$, C 49.92, H 5.00, N 11.72 %.

1,2-Diamino-3,6-dimethoxy-4,5-methylenedioxybenzene dihydrochloride (14a)

General procedure A.

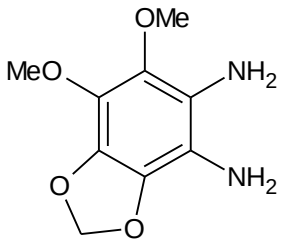
Unstable in air diamine **14a** was separated as dihydrochloride according to the following procedure. After hydrogenation (General procedure A, see above) HCl (36.5%, 7 mL) was added immediately to autoclave, the reaction mixture was removed, diluted with additional portion of HCl to pH 2 and evaporated to dryness. The residue was mixed with CH_2Cl_2 (120 mL) during 5–10 min, filtered, washed with CH_2Cl_2 (100 mL), and dried in air to afford **14a**·2HCl as brown crystals.



Yield 3.3g (63%), brown powder, mp 218–220 °C. (lit.[12] mp **14a**-base 119 °C). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.97 (4H, br. s, $2NH_2$), 6.02 (2H, s, OCH_2O), 4.03 (6H, s, $2OCH_3$). EIMS m/z 212 $[M]^+$ (100), 197 (59), 182(43), 152 (20), 126 (12), 106 (8), 96 (11), 81 (6), 68 (20). Anal. C 37.91, H 4.95, N 9.82%, calcd for $C_9H_{14}Cl_2N_2O_4$, C 37.81, H 4.90, N 9.76 %.

1,2-Diamino-3,4-dimethoxy-5,6-methylenedioxybenzene dihydrochloride (14b)

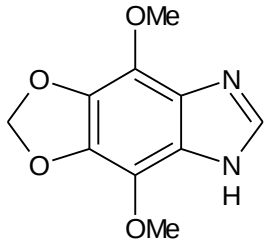
14b*2HCl was decomposed in air immediately after separation The structure was proved by mass-spectra and chemical transformation to **18b**. EIMS m/z 212 $[M]^+$.



Hydrogenation of polyalkoxynitrobenzenes 13a and 13b with cyclization. General procedure C.

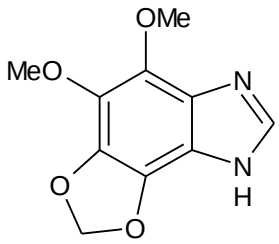
A stainless steel autoclave with block highly porous ceramic catalyst cylinder (1% Pd/6% γ-Al_2O_3) was filled with dinitrobenzene **13a** or **13b** (2.72 g, 10 mmol), $CH(OEt)_3$ (20 mL), HCOOH (6 mL). Hydrogenation was carried out at pressure of 70–80 bar for 1 h at room temperature and then for 4 h at 80 °C. The reaction mixture was cooled, removed from autoclave, the excess of $CH(OEt)_3$ and HCOOH was evaporated *in vacuo*. The residue was diluted with water (50 mL) and alkalized with NaOH (15%) to pH 9–10. The liberated solid was filtered, washed by water, dried in air, and crystallized from EtOH with activated charcoal to afford **18a** and **18b.**

4,7-Dimethoxy-5,6-methylenedioxybenzimidazole (18a)



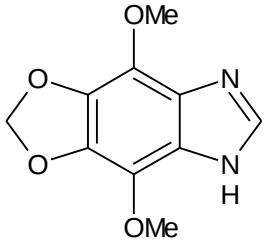
Yield 1.18 g (53%), beige powder, mp 232–234 °C ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.61 (1H, s, NH), 7.94 (1H, s, CH), 5.95 (2H, s, OCH_2O), 4.09 (3H, s, OCH_3), 3.98 (3H, s, OCH_3). ^{13}C NMR (DMSO-d_6, 125.76 MHz): δ 139.63, 133.62, 133.13, 131.26, 129.23, 124.10, 122.14, 100.99, 59.99. EIMS *m*/*z* 222 $[M]^+$ (100), 221 (37), 207 (70), 193 (15), 192(8), 178 (5), 177 (10), 145 (12), 119 (11), 79 (6). Anal. C 54.05, H 4.54, N 12.61%, calcd for $C_{10}H_{10}N_2O_4$, C 54.09, H 4.56, N 12.57 %.

6,7-Dimethoxy-4,5-methylenedioxybenzimidazole (18b)



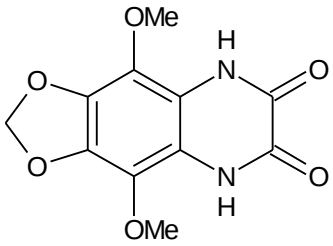
Yield 1.6 g (72%), brown powder, mp 179–181 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.65 (1H, s, NH), 8.07 (1H, s, CH), 6.03 (2H, s, OCH_2O), 3.92 (3H, s, OCH_3), 3.87 (3H, s, OCH_3). EIMS *m*/*z* 222 $[M]^+$ (88), 207 (100), 193 (12), 192(9), 177 (20), 164 (6), 149 (17), 147 (13), 134 (44), 121 (16), 119 (25), 105 (10), 94 (24), 79 (68), 67 (48). Anal. C 54.05, H 4.54, N 12.61%, calcd for $C_{10}H_{10}N_2O_4$, C 54.11, H 4.57, N 12.58 %.

Synthesis of 4,7-dimethoxy-5,6-methylenedioxybenzimidazole (18a) by cyclization of diaminobenzene (14a)



The solution of diaminobenzene dihydrochloride **14a** (5g, 17.5 mmol) in HCOOH (50 mL) was refluxed for 3 h. The volatiles were removed from the reaction mixture by evaporation *in vacuo*, the residue was diluted with water (30 mL) and alkalized with NaOH (15%) to pH 9. The separated deposit was filtered, washed with water, dried in air, and crystallized from EtOH with activated charcoal to afford **18a.** Yield 2.8g (72%).

4,9-Dimethoxy-5,8-dihydro[1,3]dioxolo[4,5-*g*]quinoxaline-6,7-dione (19a)



The solution of diaminobenzene dihydrochloride **14a** (1.28g, 4.5 mmol) and oxalic acid (0.45 g, 5 mmol) in 2N HCl (12 mL) was refluxed during 3 h, cooled to room temperature, and diluted with

cold water (30 mL). The separated deposit was filtered, washed with water (3 × 20 mL), and dried in air to afford **19a**

Yield 0.91 g (76%), cream powder, mp >300 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): □ 11.29 (2H, s, 2NH), 6.02 (2H, s, OCH_2O), 3.85 (6H, s, $2OCH_3$). EIMS *m*/*z* 266 $[M]^+$ (100), 251 (21), 237 (7), 223 (40), 193 (14), 178 (21), 94 (21), 82 (15), 79 (16). Anal. C 49.63, H 3.79, N 10.52%, calcd for $C_{11}H_{10}N_2O_6$, C 49.57, H 3.75, N 10.57 %.

X-ray analysis

The structure of the product **13a** was unambiguously established by X-ray diffraction study and is shown in Figure S1 along with the atomic numbering scheme.

The central benzo[*d*][1,3]dioxole fragment in **13a** is almost planar, excluding the C2 carbon atom which is out of the mean plane passed through the other atoms of the heterocycle by 0.217(3) Å. The two methoxy groups adopt an *anti*-periplanar conformation with the dihedral C3A─C4─O4─C8 and C7A─C7─O9─C9 angles of 35.8(2) and 41.0(2)°, respectively. The two nitro groups are also twisted relative to the benzo[*d*][1,3]dioxole ring by 66.70(10) and 40.05(12)°, respectively. The mutual conformation of the methoxy and nitro substituents can be explained by their participation in the formation of intermolecular C─H···O hydrogen bonds (see below).In the crystal, the molecules of **13a** are linked by the intermolecular C8─H8A···O7 (*x*+1, *y*+1, *z*) [C···O 3.290(3), H···O 2.57 Å, C─H···O 130°] and C9─H9A···O5 (*x*-1, *y*, *z*) [C···O 3.214(3), H···O 2.39 Å, C─H···O 141°] hydrogen bonds into layers parallel to (001) (Figure S2). It is interesting to note that the molecules of **13a** within the layers are thus oriented in the same manner. Taking the molecular structure of **13a** into account, the layers attain the polar direction toward the crystallographic ***b*** axis (Figure S2). The chiral 6_1 screw axis appears in the crystal structure of **13a** upon parallel packing of the layers along the crystallographic ***c*** axis with the consequent rotation by 60°. So, the chiral crystal structure of the non-chiral molecules of **1** confirms once again the layer-by-layer crystallization type of organic compounds described previously by Britton[13].

X-ray structure determination.

The crystal of **13a** ($C_9H_8N_2O_8$, M = 272.17) is hexagonal, space group $P6_1$, at T = 120 K: a = 9.4486(6) Å, c = 21.2784(13) Å, V = 1645.2(3) Å^3, Z = 6,

d_{calc} = 1.648 g/cm^3, $F(000)$ = 840, μ = 0.149 mm^{-1}. 25631 total reflections (3989 unique reflections, R_{int} = 0.048) were measured on a three-circle Bruker APEX-II CCD diffractometer ($\lambda(MoK_\alpha)$-radiation, graphite monochromator, φ and ω scan mode, $2\theta_{max}$ = 65.1°) and corrected for

absorption (T_{min} = 0.964; T_{max} = 0.971).[14] The structure was solved by direct methods and refined by full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The absolute structure could not be objectively determined by the refinement of Flack or Hooft parameters because the absence of heavy atoms with $Z > 14$ (Si). The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the CH_3-groups and 1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1 = 0.0394 for 3462 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.1018 for all independent reflections, S = 1.035. All calculations were carried out using the SHELXTL program.[15]

Crystallographic data for the investigated compounds have been deposited with the Cambridge Crystallographic Data Center, CCDC 1036810. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk)

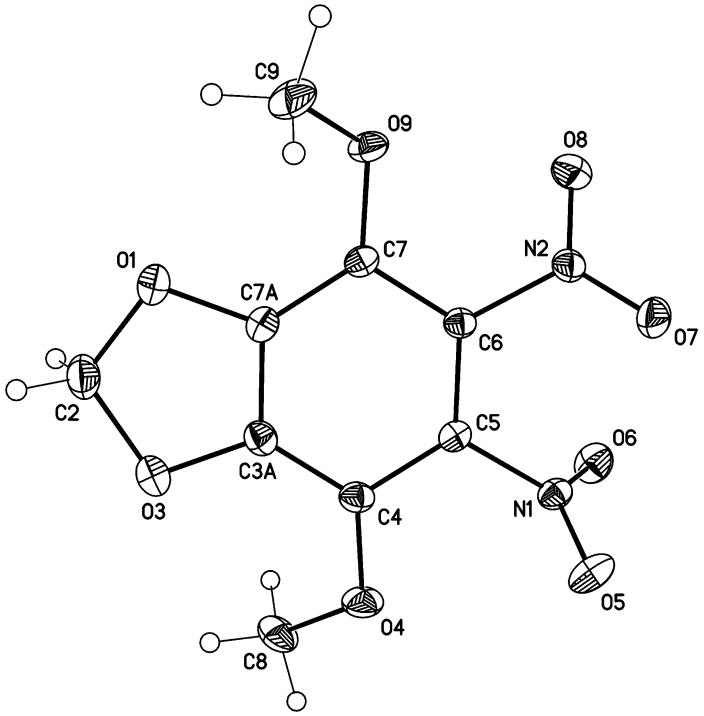


Figure S1 Molecular structure of **13a**. C3A─C4─O4─C8 and C7A─C7─O9─C9

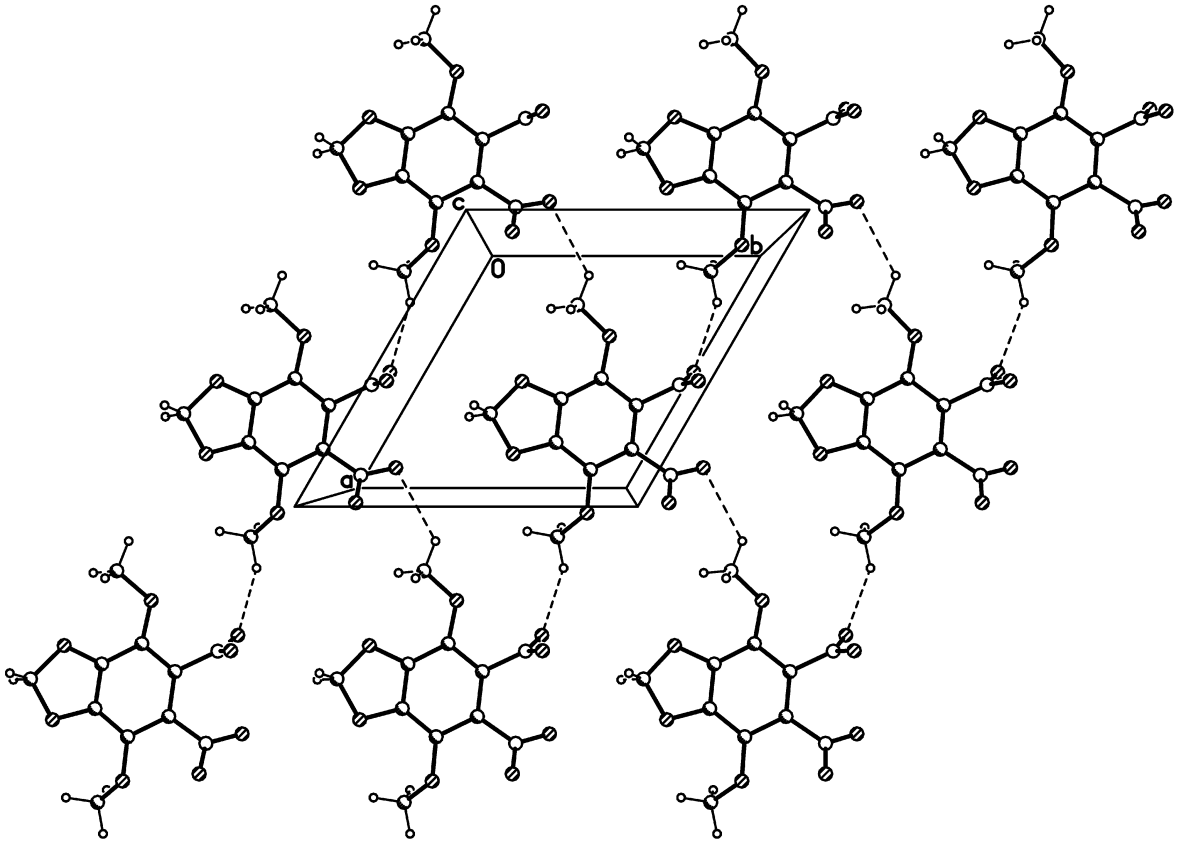


Figure S2 Crystal packing of **13a** along the ***c*** axis. Dashed lines indicate the intermolecular C─H**...**O hydrogen bonds.

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