Nucleophilic substitution of the acetoxy group in 3-methylbenzoylaminomethyl acetate

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Replacement of the acetoxy group in 3-methylbenzoylaminomethyl acetate with N- and S-nucleophiles generated from amines and thio compounds using sodium hydride gives the corresponding *N*-aminomethyl- and *N*-thiomethylbenzamides.

Key words: nucleophilic substitution of acetoxy group, sodium hydride, *N*-aminomethylbenzamides, *N*-thiomethylbenzamides, aminals, thioaminals, sulfides.

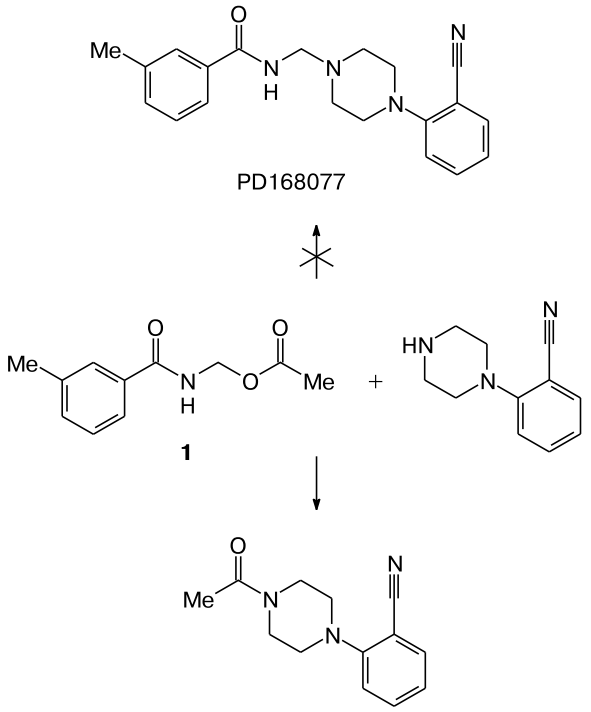
Compounds having a benzoylaminomethyl fragment in their structure are known as selective dopamine D4 receptor agonists[1,2] and are practically used in medicine.[3—5] We needed to synthesize *N*-{[4-(2-cyanophenyl)piperazin-1-yl]methyl}-3-methylbenzamide known as the PD168077 product (see Ref. 2), which is one of the representatives of this class of compounds. This compound is commonly obtained starting from derivatives of benzoylaminomethyl acetate,[1] (benzoylaminomethyl)triethylammonium chloride,[6—9] *N*-(benzoylaminomethyl)benzamide, or di(benzoylamino)methane,[10—13] as well as by aminomethylation of benzamide with the imidazole—formaldehyde system.[14]

In the present work, 3-methylbenzoylaminomethyl acetate (**1**) was chosen as the starting compound, since it is easily synthesized by acylation of glycine with 3-methylbenzoyl chloride with subsequent oxidative decarboxylation of the intermediate *N*-(3-methylbenzoyl)aminoacetic acid with lead tetraacetate.

On attempted reproduction of the described procedure[1] for the synthesis of PD168077 by the reaction of acetate **1** with 2-(1-piperazinyl)benzonitrile in the presence of triethylamine as a base, 2-(4-acetyl-1-piperazinyl)benzonitrile (the product of aminolysis of the ester group) was obtained instead of the expected compound, *i.e.*, the product of nucleophilic substitution for the acetoxy group (Scheme 1).

It is possible that other authors also met such a problem. In particular, in the work[4] a substrate with more nucleofuge triethylammonium group was used, in the work[15] sodium hydroxide was applied as a stronger base, whereas low basic amines were preliminary converted to the lithium derivatives upon treatment with butyllithium.

Scheme 1



In the present work, we showed that for providing such a deprotonation of an amine, it was reasonable to use sodium hydride. The yield of the PD168077 product was 80%, its purity was of 98%. To sum up, it was of interest to determine the scope where such transformations can be used and synthesize a number of the PD168077 analogs for further testing of their biological activity.

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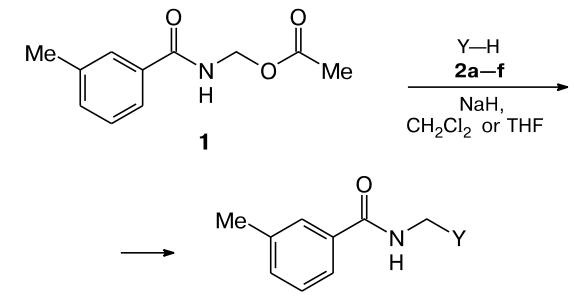
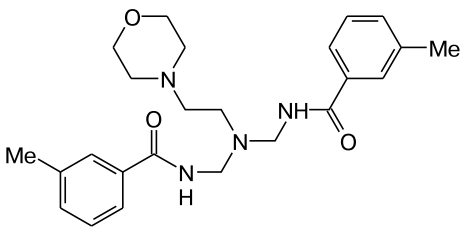
Results and Discussion

We studied a possibility of amino or mercapto groups to substitute of the acetoxy group in the aminoacetal fragment of compound **1**, using sodium hydride for deprotonation of the corresponding amines and thiols (Scheme 2, Table 1). The structures of the N- and S-nucleophiles were selected so that the products that obtained either could have served as the blocks for further synthesis or themselves were of interest as potential biologically active compounds (a probability to display biological activity was verified using the PASS program[16]). The data on the predicted and measured activity for the synthesized compounds will be published separately.

Scheme 2



Aliphatic amines **2a**—**c** reacted with aminomethyl acetate **1** to give the corresponding products **3a**—**c** in 30—68% yields. When 2-morpholinoethylamine was used, the product of disubstitution **3a´** was obtained in 38% yield together with the target compound **3a**.



3a´

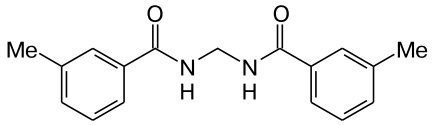
The reaction with less nucleophilic aniline **2e** reached completion only on refluxing the reaction mixture for 12 h. Its more sterically hindered isomer **2g** (see Scheme 3)

Table 1. Reactions of aminomethyl acetate **1** with amines **2a**—**e** and allyl thioglycolate **2f**

YH	Solvent	*T*/°C	*t*/h	Product	Yield (%)
2a	THF	20	0.5	**3a**	30
2b	CH_2Cl_2	20	1	**3b**	68
2c	THF	20	1	**3c**	42
2d	CH_2Cl_2	20	2	**3d**	22
2e	CH_2Cl_2	Reflux	12	**3e**	55
2f	CH_2Cl_2	20	0.5	**3f**	89

Note. *T* is the reaction temperature, *t* is the reaction time.

under similar conditions did not give the desired product and the symmetric aminal **4** was only obtained. The same product **4** was formed in the reaction of compound **1** with imidazole. In the case of 4-methylpyrazole, the yield of the target compound **3d** was only 22%. The reaction with indole led to a complex multicomponent mixture, that is apparently due to the high reactivity of positions 2 and 3 of the indole system.



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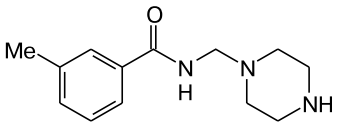
We supposed to use benzamide **3c** for its further transformation to monosubstituted piperazine **5**, which is a convenient building block for the synthesis of various benzamidomethylpiperazines. Unfortunately, even careful attempts of acidic removal of the *tert*-butoxycarbonyl group in compound **3c** with trifluoroacetic acid or HCl (cat.) in methanol at room temperature led to its decomposition and formation of symmetric aminal **4** with trace impurities of 3-methylbenzamide. It can be suggested that this is due to the instability of the aminal fragment of compound **3c** toward acids, which is susceptible to transazaacetalization. We also detected slow decomposition of the starting aminoacetal **1** to aminal **4** and 3-methylbenzamide on standing even at –20 °C.

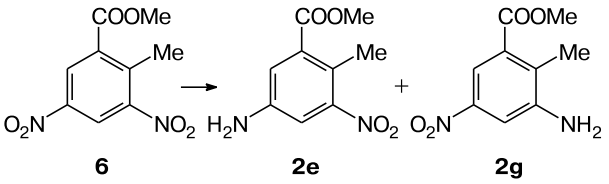


5

The synthesis of isomeric anilines **2e,g** from methyl 2-methyl-3,5-dinitrobenzoate (**6**) should be considered separately (Scheme 3). We succeeded in finding such reaction conditions, under which anilines **2e** or **2g** were the dominating products. For instance, in the case of catalytic (Pd/C) reduction with formic acid, the ratio of isomers **2e** and **2g** was 4 : 1. When metallic iron in acetic acid was

used as a reducing agent, this ratio was 1 : 4. The synthesis of isomer **2e** has been described earlier,[17] however, attempted reproduction of this procedure led to a mixture of the starting compound **6** and five other difficult to isolate components.

Scheme 3



The mercapto group in allyl thioglycolate has proved reactive enough under such conditions, and the yield of sulfide **3f** was 89% (see Scheme 2). In the case of thio compounds **2h,i** of more complicated structure and disposed to thioamide-iminothiol tautomerism, both reaction centers of the ambident nucleophile reacted with acetoxymethylbenzamide **1** (Scheme 4). In the case of 2,4-dihydro-3*H*-1,2,4-triazole-3-thione (**2h**), a disubstituted product **3h** was isolated in 19% yield. The reaction with 1,3-dihydro-2*H*-benzimidazole-2-thione (**2i**) led to a mixture, from which 3-methylbenzamide, aminal **4**, and unreacted acetoxymethylbenzamide **1** were only isolated by preparative chromatography. Analysis of other products were performed by LC-MS, which indicated the presence of ions with m/z 445 $[M + H]^+$ and 298 $[M - CH_3C_6H_4CONHCH_2 + H]^+$. The latter can be assigned to the target product with the structure suggested as **3i**. In all the cases studied, substitution for the acetoxy group did not occur without addition of NaH.

In conclusion, the studies performed showed that the acetoxy group in the aminoacetyl fragment of 3-methylbenzoylaminomethyl acetate can be substituted for by the S_N2 mechanism when strong enough N- and S-nucleophiles are used, namely, the amine and thiol sodium derivatives. The results obtained can be used in medicinal chemistry and screening programs.

Experimental

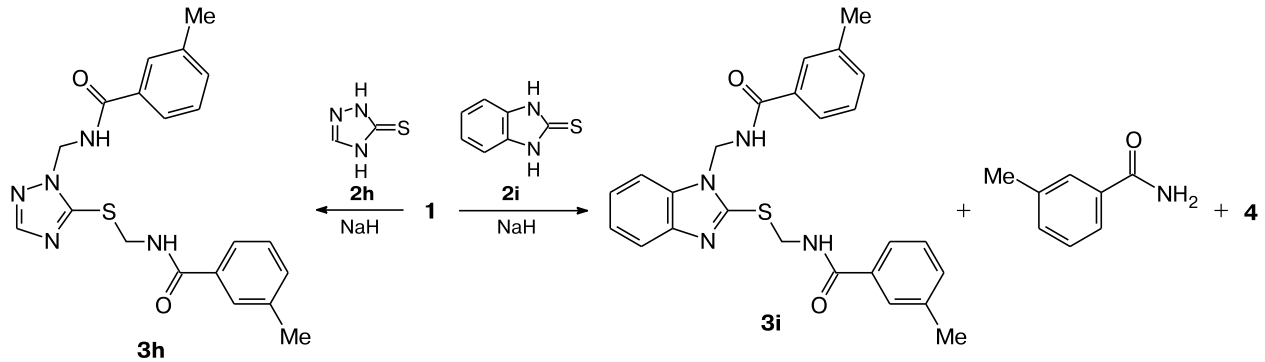
Reaction progress was monitored by thin-layer chromatography on Merck Silica gel 60 F_{254} plates. Preparative chromatography was performed on columns with silica gel Fluka Silica Gel 60 (0.04—0.063 mm). Melting points were determined on a Gallenkamp apparatus and were not corrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Inova spectrometer (300 and 75 MHz, respectively) in DMSO-d_6 or $CDCl_3$. IR spectra were recorded on a Perkin—Elmer BX FT-IR spectrometer in KBr pellets. Mass spectra were recorded on a Micromass UK Quattro Ultima Pt instrument.

Synthesis of compounds 3a—f (general procedure). 3-Methylbenzoylaminomethyl acetate (**1**) (1 g, 4.8 mmol) and the corresponding reactant **2** (4.8 mmol) were dissolved in dichloromethane or THF (10 mL) (see Table 1), followed by addition of sodium hydride (9.6 mmol, 0.23 g of 60% dispersion in mineral oil), the mixture was stirred for 0.5—12 h at a given temperature, monitoring the reaction course by TLC. After the full conversion of the starting compound **1** was reached, the reaction mixture was poured into water (200 mL) and extracted with dichloromethane (100 mL). The organic layer was dried with anhydrous sodium sulfate, concentrated *in vacuo*, and treated as indicated further.

***N*-{[4-(2-Cyanophenyl)piperazin-1-yl]methyl}-3-methylbenzamide (PD168077).** The oil that obtained was dissolved in hot propan-2-ol (4 mL) and mixed with a solution of maleic acid (1 g) in hot propan-2-ol (6 mL), then cooled, and filtered to obtain white crystalline compound (3.64 g, 80%) 98% in purity. ^{1}H NMR is identical to that described earlier.[1]

4-{2-[(3-Methylbenzoylaminomethyl)amino]ethyl}morpholine (3a) and **4-{2-[*N,N*-bis(3-methylbenzoylaminomethyl)amino]-ethyl}morpholine (3a′)** were separated by chromatography (eluent dichloromethane—methanol (3 : 2)), R_f 0.35 and 0.50, respectively. Compound **3a**. The yield was 0.20 g (30%), oil. ^{1}H NMR ($CDCl_3$), δ: 2.24 (m, 7 H, $ArCH_3$, $N(CH_2)_2$); 2.33 (t, 2 H, $CH_2N(CH_2)_2$, J = 6.0 Hz); 2.67 (t, 2 H, $CH_2CH_2N(CH_2)_2$, J = 6.0 Hz); 3.54 (m, 4 H, $O(CH_2)_2$); 4.25 (d, 2 H, $CONHCH_2$, J = 6.0 Hz); 7.17 (m, 2 H, H_{Ar}); 7.50 (m, 3 H, NH, H_{Ar}). ^{13}C NMR ($CDCl_3$), δ: 21.6, 42.8, 53.8, 55.6, 58.7, 67.0, 124.2, 128.0, 128.6, 132.5, 134.5, 138.5, 168.6. IR, ν/cm^{-1}: 1643 (CO);

Scheme 4



3313 (NH). Found (%): C, 65.11; H, 8.21; N, 15.39. $C_{15}H_{23}N_3O_2$. Calculated (%): C, 64.95; H, 8.36; N, 15.15. Compound **3a´**. The yield was 0.31 g (38%), oil. ^{1}H NMR ($CDCl_3$), δ: 2.34 (s, 6 H, 2 $ArCH_3$); 2.50 (t, 4 H, $N(CH_2)_2$, J = 4.2 Hz); 2.61 (t, 2 H, $(CH_2NH)_2NCH_2$, J = 5.1 Hz); 2.92 (t, 2 H, $(CH_2NH)_2NCH_2CH_2$, J = 5.4 Hz); 3.70 (t, 4 H, $O(CH_2)_2$, J = 4.5 Hz); 4.50 (d, 4 H, 2 $CONHCH_2$, J = 6.6 Hz); 7.28—7.34 (m, 4 H, H_{Ar}); 7.58—7.61 (m, 4 H, H_{Ar}); 7.93 (t, 2 H, 2 $NHCH_2$, J = 6.3 Hz). ^{13}C NMR ($CDCl_3$), δ: 21.5, 45.9, 54.2, 57.4, 57.5, 67.0, 124.5, 128.1, 128.7, 132.8, 134.2, 138.6, 169.1. IR, ν/cm^{-1}: 1644; 1645 (CO); 3334 (NH). Found (%): C, 68.18; H, 7.84; N, 12.97. $C_{24}H_{32}N_4O_3$. Calculated (%): C, 67.90; H, 7.60; N, 13.20.

3-Methyl-*N*-(morpholin-4-ylmethyl)benzamide (3b) was isolated by chromatography (eluent dichloromethane—ethyl acetate (1 : 1)), R_f 0.1. The yield was 0.76 g (68%), oil. ^{1}H NMR ($CDCl_3$), δ: 2.41 (s, 3 H, $ArCH_3$); 2.65 (t, 4 H, $N(CH_2)_2$, J = 4.5 Hz); 3.73 (t, 4 H, $O(CH_2)_2$, J = 4.5 Hz); 4.30 (d, 2 H, $NHCH_2$, J = 6.3 Hz); 6.70 (m, 1 H, $NHCH_2$); 7.33—7.35 (m, 2 H, H_{Ar}); 7.57—7.63 (m, 2 H, H_{Ar}). ^{13}C NMR ($CDCl_3$), δ: 21.6, 50.7, 62.1, 67.0, 124.2, 128.0, 128.8, 132.8, 134.3, 138.8, 168.5. IR, ν/cm^{-1}: 1667 (CO); 3386 (NH). Found (%): C, 66.74; H, 7.63; N, 12.22. $C_{13}H_{18}N_2O_2$. Calculated (%): C, 66.64; H, 7.74; N, 11.96.

1-*tert*-Butoxycarbonyl-4-[(3-methylbenzoylamino)methyl]-piperazine (3c) was isolated by chromatography (eluent dichloromethane—ethyl acetate (1 : 1)), R_f 0.15. The yield was 0.66 g (42%), crystalline compound, m.p. 123—125 °C. ^{1}H NMR ($CDCl_3$), δ: 1.48 (s, 9 H, $C(CH_3)_3$); 2.44 (s, 3 H, $ArCH_3$); 2.61 (t, 4 H, $N(CH_2)_2$, J = 10.2 Hz); 3.48 (t, 4 H, $CON(CH_2)_2$, J = 9.9 Hz); 4.36 (d, 2 H, $NHCH_2$, J = 6.3 Hz); 6.54 (m, 1 H, $NHCH_2$); 7.35—7.37 (m, 2 H, H_{Ar}); 7.59—7.64 (m, 2 H, H_{Ar}). ^{13}C NMR ($CDCl_3$), δ: 21.6, 28.6, 43.3, 51.1, 61.8, 80.0, 124.3, 128.1, 128.7, 132.7, 134.3, 138.6, 154.9, 168.7. IR, ν/cm^{-1}: 1673 (CO); 3386 (NH). Found (%): C, 65.08; H, 8.52; N, 12.31. $C_{18}H_{27}N_3O_3$. Calculated (%): C, 64.84; H, 8.16; N, 12.60.

3-Methyl-*N*-[(4-methyl-1*H*-pyrazol-1-yl)methyl]benzamide (3d) was isolated by crystallization from hexane. The yield was 0.25 g (22%), m.p. 121—123 °C, R_f 0.5 (dichloromethane—ethyl acetate (1 : 1)). ^{1}H NMR ($CDCl_3$), δ: 2.07 (s, 3 H, CH_3); 2.33 (s, 3 H, $ArCH_3$); 5.67 (d, 2 H, $NHCH_2$, J = 6.3 Hz); 7.27—7.64 (m, 6 H, CH); 8.71 (m, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 9.1, 21.5, 55.2, 117.0, 124.6, 128.3, 128.6, 130.2, 133.0, 133.4, 138.4, 140.6, 168.4. IR, ν/cm^{-1}: 1662 (CO); 3256 (NH). Found (%): C, 68.21; H, 6.82; N, 18.34. $C_{13}H_{15}N_3O$. Calculated (%): C, 68.10; H, 6.59; N, 18.33.

Methyl 2-methyl-5-[(3-methylbenzoylaminomethyl)amino]-3-nitrobenzoate (3e). The reaction was carried out by reflux in dichloromethane for 12 h. The product was isolated by chromatography (eluent dichloromethane—ethyl acetate (19 : 1)), R_f 0.25. The yield was 0.48 g (55%), crystalline compound, m.p. 105—107 °C. ^{1}H NMR ($CDCl_3$), δ: 2.36 (s, 3 H, $ArCH_3$); 2.45 (s, 3 H, $ArCH_3$); 3.91 (s, 3 H, OCH_3); 4.90—4.94 (m, 2 H, $NHCH_2$); 5.26 (m, 1 H, ArNH); 7.26—7.35 (m, 5 H, H_{Ar}); 7.52—7.58 (m, 2 H, CONH, H_{Ar}). ^{13}C NMR ($CDCl_3$), δ: 15.6, 21.5, 49.8, 52.8, 110.8, 119.4, 121.8, 124.3, 128.0, 128.8, 133.0, 133.7, 134.3, 138.8, 144.5, 152.8, 167.5, 169.1. IR, ν/cm^{-1}: 1642, 1726 (CO); 3365 (NH). Found (%): C, 60.31; H, 5.57; N, 12.02. $C_{18}H_{19}N_3O_5$. Calculated (%): C, 60.56; H, 5.36; N, 11.76.

Allyl 2-[(3-methylbenzoylaminomethyl)sulfanyl]acetate (3f) was isolated by chromatography (eluent dichloromethane—ethyl acetate (1 : 1)), R_f 0.88. The yield was 1.34 g (89%), oil. ^{1}H NMR ($CDCl_3$), δ: 2.39 (s, 3 H, $ArCH_3$); 3.45 (s, 2 H, SCH_2CO); 4.59—4.61 (m, 2 H, $COOCH_2$); 4.70 (d, 2 H, $NHCH_2$, J = 6.3 Hz); 5.19—5.34 (m, 2 H, OCH_2CHCH_2); 5.80—5.93 (m, 1 H, OCH_2CH); 7.28—7.64 (m, 5 H, H_{Ar}, NH). ^{13}C NMR ($CDCl_3$), δ: 20.9, 33.8, 42.9, 65.9, 118.6, 123.5, 127.4, 128.0, 128.1, 130.9, 132.1, 138.0, 166.8, 170.8. IR, ν/cm^{-1}: 1646, 1733 (CO); 3322 (NH). Found (%): C, 60.56; H, 6.44; N, 4.83. $C_{14}H_{17}NO_3S$. Calculated (%): C, 60.19; H, 6.13; N, 5.01.

1-(3-Methylbenzoylaminomethyl)-5-[(3-methylbenzoylamino-methyl)sulfanyl]-1*H*-1,2,4-triazole (3h). The reaction was carried out by reflux in dichloromethane for 7 h. The product was isolated by chromatography (eluent dichloromethane—ethyl acetate (1 : 2)), R_f 0.2. The yield was 0.18 g (19%), oil. ^{1}H NMR ($CDCl_3$), δ: 2.30, 2.31 (both s, 6 H, 2 $ArCH_3$); 5.01 (d, 2 H, $NHCH_2S$, J = 6.6 Hz); 5.65 (d, 2 H, $NHCH_2N$, J = 6.6 Hz); 7.19—7.30 (m, 4 H, H_{Ar}); 7.48—7.61 (m, 4 H, H_{Ar}); 7.92 (t, 1 H, $NHCH_2S$, J = 6.6 Hz); 8.25 (t, 1 H, $NHCH_2N$, J = 6.6 Hz); 8.42 (s, 1 H, CH triazole). IR, ν/cm^{-1}: 1654 (CO); 3346, 3407 (NH). Found (%): C, 61.02; H, 5.61; N, 17.52. $C_{20}H_{21}N_5O_2S$. Calculated (%): C, 60.74; H, 5.35; N, 17.71.

Methyl 5-amino-2-methyl-3-nitrobenzoate (2e). A solution of 85% aqueous formic acid (36 mL, 1.12 mol) in acetonitrile (80 mL) was slowly added to a cooled with ice solution of triethylamine (80 mL, 0.57 mol) in acetonitrile (80 mL). The solution that formed was cooled to 0—5 °C, followed by addition of methyl 2-methyl-3,5-dinitrobenzoate (**6**) (40 g, 0.17 mol) and 10% Pd/C (1.2 g). The reaction mixture was stirred for 12 h with cooling in an ice bath and additionally for 3 days at room temperature, then it was filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane, washed with water and saturated aq. sodium carbonate, dried with anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was twice recrystallized from toluene. The yield was 14.3 g (41%), m.p. 135—137 °C (agrees with the data in Ref. 17), R_f 0.3 (dichloromethane—ethyl acetate (10 : 1)).

Methyl 3-amino-2-methyl-5-nitrobenzoate (2g). Methyl 2-methyl-3,5-dinitrobenzoate (**6**) (0.5 g, 2.1 mol) and iron powder (0.5 g, 8.9 mol) were added to the boiling acetic acid. After the exothermic reaction began, the heating was removed. After dinitro compound **6** was completely consumed, the reaction mixture was poured on ice and filtered. A precipitate was dissolved in dichloromethane, washed with water and saturated aq. sodium carbonate, dried with anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was recrystallized from methanol. The yield was 0.22 g (50%), m.p. 145—147 °C, R_f 0.65 (dichloromethane—ethyl acetate (19 : 1)). ^{1}H NMR ($CDCl_3$), δ: 2.41 (s, 3 H, $ArCH_3$); 3.91 (s, 3 H, OCH_3); 4.11 (s, 2 H, NH_2); 7.61 (m, 1 H, H_{Ar}); 8.04 (m, 1 H, H_{Ar}). ^{13}C NMR ($CDCl_3$), δ: 14.6, 52.8, 111.3, 115.0, 130.4, 132.36, 146.4, 147.0, 167.4. IR, ν/cm^{-1}: 1717 (CO); 3391, 3476 (NH_2). Found (%): C, 51.58; H, 4.92; N, 13.18. $C_9H_{10}N_2O_4$. Calculated (%): C, 51.43; H, 4.80; N, 13.33.

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References

1. S. A. Glase, H. C. Akunne, L. M. Georgic, T. G. Heffner, R. G. MacKenzie, P. J. Manley, T. A. Pugsley, L. D. Wise, *J. Med. Chem.*, 1997, 1771.

2. M. V. Patel, T. Kolasa, K. Mortell, M. A. Matulenko, A. A. Hakeem, J. J. Rohde, S. L. Nelson, M. D. Cowart, M. Nakane, L. N. Miller, M. E. Uchic, M. A. Terranova, O. F. El-Kouhen, D. L. Donelly-Roberts, M. T. Namovic, P. R. Hollingsworth, R. Chang, B. R. Martino, J. M. Wetter, K. C. Marsh, R. Martin, J. F. Darbyshire, G. Gintant, G. C. Hsieh, R. B. Moreland, J. P. Sullivan, J. D. Brioni, A. O. Stewart, *J. Med. Chem.*, 2006, 7450.
3. F. I. Tarazi, R. J. Baldessarini, *Mol. Psychiatry*, 1999, **4**, 529; L. J. Bristow, M. S. Kramer, J. Kulagowski, S. Patel, C. I. Ragan, G. R. Seabrook, *Trends Pharmacol. Sci.*, 1997, **18**, 186.
4. R. P. Ebstein, R. H. Belmaker, *Mol. Psychiatry*, 1997, **2**, 381; K. Boór, Z. Rónai, Z. Nemoda, P. Gaszner, M. Sasvári-Székely, A. Guttman, H. Kalász, *Curr. Med. Chem.*, 2002, **9**, 793; S. B. Powell, M. P. Paulus, D. S. Hartman, T. Godel, *Neuropharmacology*, 2003, **44**, 473.
5. K.-E. Andersson, *Pharmacol. Rev.*, 2001, **53**, 417; M. Zarrindast, S. Shokravi, M. Samini, *Gen. Pharmacol.*, 1992, **23**, 671.
6. E. Popovski, L. Klisarova, D. Vikic-Topic, *Molecules*, 2000, 927.
7. E. Popovski, J. Bogdanov, M. Najodski, *Molecules*, 2006, 279.
8. A. Mateska, G. Stojkovic, B. Mikhova, K. Mladenovska, E. Popovski, *ARKIVOC*, 2009, **x**, 131.
9. P. Csomós, L. Fodor, G. Bernáth, A. Csámpai, P. Sohár, *Tetrahedron*, 2009, **65**, 1475.
10. P. Csomós, L. Fodor, G. Bernáth, A. Csámpai, P. Sohár, *Tetrahedron*, 2008, **64**, 8646.
11. B. P. Branchaud, P. Tsai, *J. Org. Chem.*, 1989, 5475.
12. H. R. Snyder, J. H. Brewster, *J. Am. Chem. Soc.*, 1949, 1058.
13. M. Sekiya, N. Yanahira, M. Tanaka, *Chem. Pharm. Bull.*, 1984, **12**, 440.
14. J. Pernak, B. Mrowczynski, J. Weglewski, *Synthesis*, 1994, 1415.
15. M. Hashimoto, S. Niwata, S. Iwata, H. Fukami, *Chem. Express.*, 1992, **7**, 65.
16. http://195.178.207.233/PASS/.
17. J. G. Cannon, T. Lee, M. Ilhan, J. Koons, J. P. Long, *J. Med. Chem.*, 1984, 386.

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