Chemistry of Heterocyclic Compounds, Vol. 44, No. 1, 2008

METHYL NITROACETATE AND 3-NITROPROPIONATE IN THE SYNTHESIS OF HEXAHYDROPYRIMIDINES AND PIPERIDINES

R. R. Shakirov[1], T. V. Dokichev[2], R. Z. Biglova[2], N. M. Vlasova[1], N. Z. Baibulatova[1], and R. F. Talipov[2]

Treatment of methyl nitroacetate and 3-nitropropionate with formaldehyde and primary amines under Mannich reaction conditions gives 5-nitrohexahydropyrimidines. In the case of methyl nitroacetate both the 5-nitrohexahydropyrimidine and isomeric 3,5-di(methoxycarbonyl)-1-methyl-3,5-dinitropiperidines are formed.

Keywords: hexahydropyrimidines, 3,5-dinitropiperidines, methyl nitrocarboxylates, Mannich reaction.

The reaction of primary amines and formaldehyde with compounds containing a mobile hydrogen atom on a carbon atom is widely used in organic synthesis as a convenient method for preparing tetrahydro-1,3-oxazines, hexahydropyrimidines [1, 2], and also 3-aza- [3-6] and 3,7-diazabicyclo[3,3,1]nonanes [3, 7-15]. Members of this class of compounds show high physiological activity and are used in medical practice as antimicrobial, antiviral, antitumor and other medicinal agents [10-12, 16]. It is known that nitro–substituted heterocyclic compounds show increased antibacterial activity [1], can behave as sources of nitric oxide [17] in the human organism, and they are of interest both as chemotherapeutic agents and as intermediates in organic synthesis. Hence 5-[2-(methoxycarbonyl)ethyl]-1,3-dimethyl-5-nitrohexahydropyrimidine shows clear anti-arrythmic activity [18] and trinitrohexahydropyrimidine (containing a glutaric acid fragment) is a convenient synthon for preparing immunologically active peptide conjugates [19] used in immunoenzymic analysis.

Condensation with a nitro compound has shown promise in the synthesis of novel, practically important polyfunctional six–membered nitrogen heterocycles. According to literature data the course of the reaction of aliphatic mononitroalkanes with formaldehyde and primary amines depends on the structure of the starting reagents, their ratio, the temperature, and the nature of the solvent and it can occur to form amines, diaminopropanes, tetrahydrooxazines, and hexahydropyrimidines [1, 2]. It has been shown previously that the reaction of methyl 4-nitrobutanoate with methylamine hydrochloride and CH_2O occurs in 40% yield to give 5-nitro-5-[2-(methoxycarbonyl)ethyl]-1,3-dimethyl-hexahydropyrimidine and it is formed exclusively *via* the CH_2NO_2 fragment of the starting nitrobutanoate [18].

---

[1]Institute of Organic Chemistry, Ufa Science Center of the Russian Academy of Sciences, Ufa 450054, Russia; e-mail: dokichev@anrb.ru. [2]Bashkir State University, Ufa 450074, Russia; e-mail: interdpt@bsu.bashedu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 53-60, January, 2008. Original article submitted March 9, 2007.

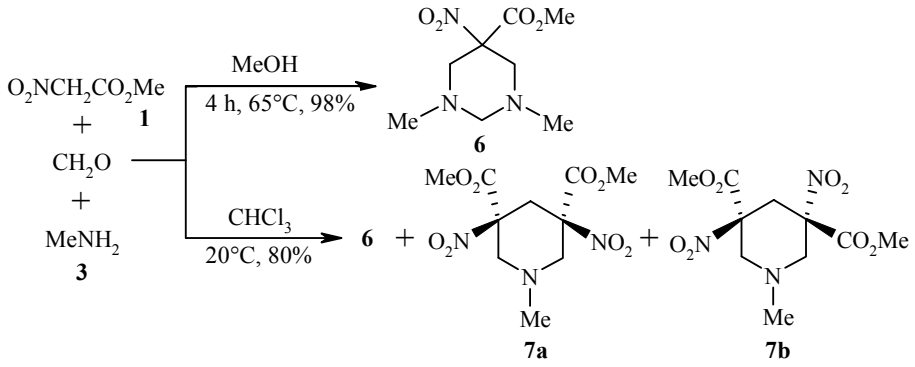
0009-3122/08/4401-0043©2008 Springer Science+Business Media, Inc.

In this work we report the synthesis of a series of nitro-substituted hexahydropyrimidines and piperidines *via* the condensation of methyl nitroacetate or 3-nitropropionate with formaldehyde and primary amines under Mannich reaction conditions and a study of the effect of the structure of the starting components and reaction conditions on the yield and composition of the products formed. It should be stressed that this work is of interest in a scheme of developing novel routes to amino acids of synthetic origin.

Methyl nitroacetate (**1**) and 3-nitropropionate (**2**) were used as the nitrocarboxylic esters and methyl- (**3**), isopropyl- (**4**), and benzylamine (**5**) as the primary amines. Experiments were carried out by refluxing in methanol for 4 h with a 1:10:5 molar ratio of the methyl nitrocarboxylate, formaldehyde, and amine. In these chosen conditions it was found the methyl nitroacetate **1** reacts with formaldehyde (as a 35% formalin solution) and 25% methylamine to give a 98% yield of 5-(methoxycarbonyl)-1,3-dimethyl-5-nitrohexahydropyrimidine (**6**) with high selectivity. It should be noted that 5-nitrohexahydropyridines were prepared in the study [20] in two stages from ethyl nitroacetate.

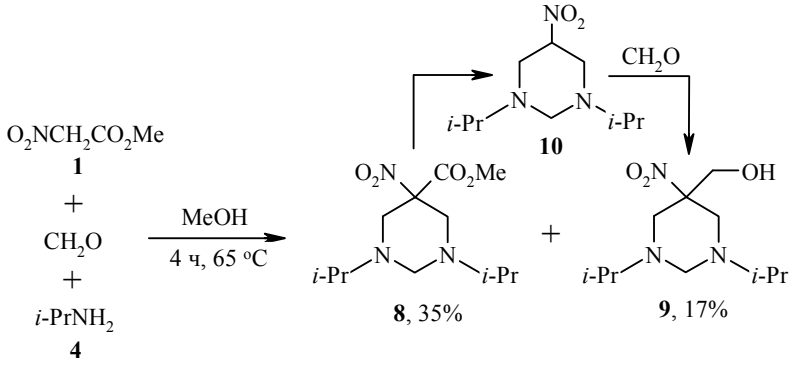
The route of condensation of methyl nitroacetate **1** depends markedly on the nature of the solvent (Scheme 1). Hence use of chloroform lowers the reaction selectivity and gives the hexahydropyrimidine (**6**) together with the 3,5-dimethoxycarbonyl-1-methyl-3,5-dinitropiperidines (**7**) in overall yield 80% and in the ratio 3:1. According to ^{1}H and ^{13}C NMR data the piperidine **7** exists as a 1:1 mixture of the two diastereomers **7a,b** differing in the *cis* and *trans* positioning of the NO_2 groups.

Scheme 1



The reaction of methyl nitroacetate **1** with isopropylamine **4** and formaldehyde in methanol (Scheme 2) gives the expected hexahydropyrimidine **8** along with the 5-hydroxymethyl-5-nitrohexahydropyrimidine (**9**) in 35 and 17% yield respectively. The nitro alcohol **9** is likely formed as a result of hydrolysis

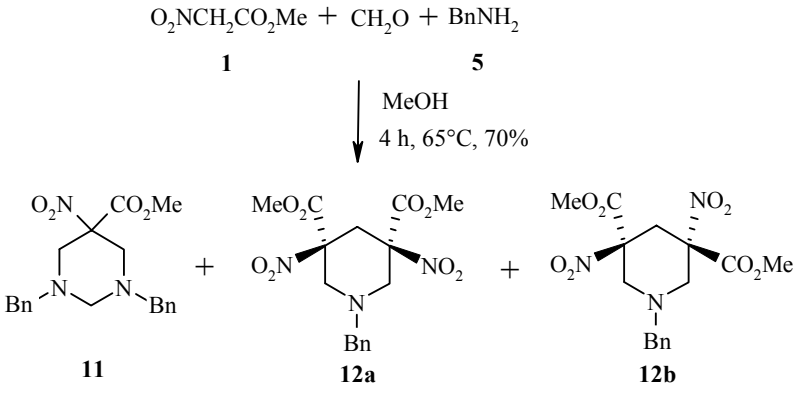
Scheme 2



and decarboxylation of compound **8** and subsequent reaction of the 1,3-diisopropyl-5-nitrohexahydropyrimidine (**10**) formed with a molecule of formaldehyde *via* a Henry reaction [21, 22]. The structure of the hexahydropyrimidine **9** was identified from ^{1}H and ^{13}C NMR spectroscopic data. The methylene protons in the CH_2OH group appear in the ^{1}H NMR spectrum as a singlet at 4.0 ppm and the presence of this hydroxymethyl group is also confirmed by the carbon atom signal for the CH_2OH fragment at 66.0 ppm in the ^{13}C NMR spectrum.

A study of the effect of the nature of the starting reagents on the reaction route showed a marked dependence on the amine component. Hence, by contrast with methylamine and isopropylamine, the condensation of the methyl nitroacetate **1** with benzylamine **5** and CH_2O occurs nonselectively upon refluxing in methanol (Scheme 3) to give an overall yield of 70% of a mixture of 1,3-dibenzyl-5-methoxycarbonyl-5-nitrohexahydropyrimidine (**11**), and *cis*- **12a** and *trans*-3,5-bis(methoxycarbonyl)-3,5-dinitropiperidine (**12b)** in the ratio 6:1:1 which were separated using column chromatography. The ratio of the isomers **12a** and **12b** was determined from the ^{1}H NMR spectrum of the reaction mixture based on the integrated intensities of the OMe group proton signals, the chemical shifts of which are 3.79 and 3.81 ppm.

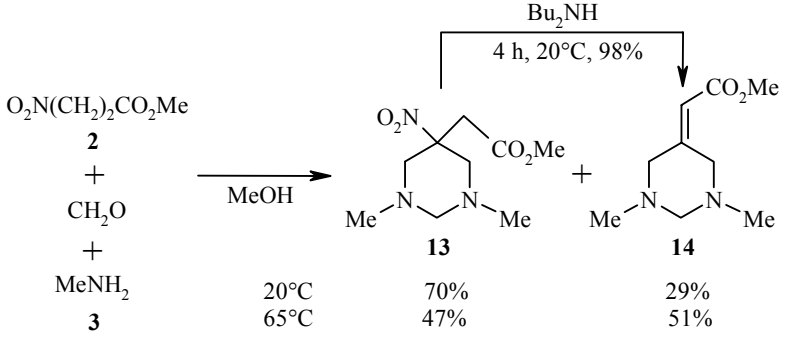
Scheme 3



11 : **12a** : **12b** = 6 : 1 : 1

In the case of the methyl 3-nitropropionate **2** the formation of a piperidine fragment was not observed under the Mannich reaction conditions. The reaction of the methyl 3-nitropropionate **2** with methylamine and formaldehyde in methanol at 65ºC over 4 h gave the 5-methoxycarbonylmethyl-1,3-dimethyl-5-nitrohexahydropyrimidine (**13**) and 5-methoxycarbonylmethylidene-1,3-dimethyl-hexahydropyrimidine (**14**) in 47 and 51% yields respectively. Lowering the temperature to 20ºC led to an increase in the yield of heterocycle **13** to 70% (Scheme 4).

Scheme 4



Formation of the unsaturated compound **14** is in agreement with literature data [23] and occurs at pH 7-8 under the action of methylamine as a result of separation of nitrous acid from the hexahydropyrimidine molecule **13** which contains an active methylene group in an α-position to the CO_2Me group. It was found experimentally that stirring the hexahydropyrimidine **13** in dibutylamine taken as the base gives a quantitative yield of the heterocycle **14**.

The structure of the synthesized compounds separated by column chromatography was confirmed from their ^1H and ^{13}C NMR spectroscopic data using the homo- and heteronuclear HH COSY and CH CORR methods. The ^{13}C NMR spectra of the hexahydropyrimidines **6, 8, 9, 11, 13, 14** show characteristic signals for the NCH_2N group carbon atoms in the range 70.3-78.5 ppm. The signal at 77.4 ppm in the carbon spectrum of the 5-methoxycarbonyl-1,3-dimethyl-5-nitrohexahydropyrimidine **6** for the NCH_2N fragment correspond to the axial and equatorial protons seen at 2.72 and 3.35 ppm respectively in the proton spectrum.

Hence a one-pot method has been developed for the synthesis of hexahydropyrimidines and 3,5-dinitropiperidines *via* reaction of methyl nitrocarboxylates with formaldehyde and primary amines. It was found that the reaction route depends of the structure of the starting reagents and the conditions used.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75 MHz respectively) using $CDCl_3$ and with TMS as internal standard. IR spectra were obtained on a Specord M-80 instrument as a thin film and mass spectra on an MX-1300 spectrometer with an inlet system heated at 100ºC and ionizing intensities of 12 and 70 eV. GLC Analysis was performed on a Chrom-5 chromatograph with flame ionization detection (column 1200×5 mm, 5% SE-30 on Inerton N-AW DMCS (0.125-0.160 mm, and helium gas carrier). Elemental analysis was performed on an HEKAtech Gmbh Analysen-technik's Euro-EA CHN analyzer. TLC was performed on Merck Silufol plates. Preparative separations were carried out using column chromatography on SiO_2 from the Lancaster company (70-230 mesh).

Methyl 2-nitroacetate (**1**) and 3-nitropropionate (**2**) were synthesized by known methods [24, 25].

Reaction of Methyl Nitroacetate and 3-Nitropropionate with Formaldehyde and Primary Amines (General Method). Formalin (2.93 ml, 35%, 37.6 mmol of CH_2O) and the primary amine (18.8 mmol) were added to a solution of the methyl nitrocarboxylate (3.76 mmol) in MeOH (27 ml) which was stirred with a magnetic stirrer and the product was refluxed with a reflux condenser for 4 h. Methanol was distilled off under reduced pressure and chloroform (18 ml) was added. The reaction mixture was washed with water (3×10 ml), dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel column (eluent $CHCl_3$–2-PrOH, 9:1).

5-Methoxycarbonyl-1,3-dimethyl-5-nitrohexahydropyrimidine (6) was obtained at 65ºC from methyl nitroacetate **1**, (10 g, 8.4 mmol), aqueous formalin (35%, 6.99 ml, 84 mmol), and aqueous methylamine (25.2%, 5.17 g, 42 mmol) as an oil (1.81 g, 98%). IR spectrum, ν, cm^{-1}: 1384, 1552 (NO_2), 1284, 1712 (CO_2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.28 (6H, s, $2CH_3$); 2.72 ($1H_{ax}$, d, ^2J = 9.2, NCH_2N); 2.77 ($2H_{ax}$, d, ^2J = 12.6, $2CH_2N$); 3.35 ($1H_{eq}$, d, ^2J = 9.2, NCH_2N); 3.56 ($2H_{eq}$, d, ^2J = 12.6, $2CH_2N$); 3.77 (3H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 42.2 (NCH_3); 53.79 (OCH_3); 56.8 (CH_2N); 77.4 (NCH_2N); 89.0 (CNO_2); 164.9 (CO_2). Mass spectrum, *m/z*: 217 $[M]^+$. Found, %: C 44.35; H 7.00; N 19.20. $C_8H_{15}N_3O_4$. Calculated, %: C 44.23; H 6.96; N 19.34.

When carrying out the reaction in chloroform (20ºC, 4 h) the yield of the hexahydropyrimidine **6** was 48% together with the piperidines **7a** and **7b** in 32% overall yield.

***cis*-3,5-Bis(methoxycarbonyl)-1-methyl- (7a) and *trans*-3,5-Bis(methoxycarbonyl)-1-methyl-3,5-dinitropiperidines (7b)**. IR spectrum, ν, cm^{-1}: 1540 (NO_2), 1738 (C=O). Mass spectrum, *m/z*: 305 $[M]^+$. Found, %: C 39.10; H 4.95; N 13.77. $C_{10}H_{15}N_3O_8$. Calculated, %: C 39.35; H 4.95; N 13.77.

***cis*-3,5-Di(methoxycarbonyl)-1-methyl-3,5-dinitropiperidine (7a)**. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.42 (3H, s, NCH_3); 2.78 ($2H_{ax}$, d, ^2J = 13.2, $2CH_2N$); 3.18 ($1H_{ax}$, d, ^2J = 16.2, CH_2); 3.52 ($2H_{eq}$, d, ^2J = 13.2, $2CH_2N$); 3.63 ($1H_{eq}$, d, ^2J = 16.2, CH_2); 3.84 (6H, s, $2OCH_3$). ^{13}C NMR spectrum, δ, ppm: 33.4 (CH_2); 45.2 (NCH_3); 54.3 (OCH_3); 58.1 (CH_2N); 88.9 (CNO_2); 165.3 (CO_2).

***trans*-3,5-Di(methoxycarbonyl)-1-methyl-3,5-dinitropiperidine (7b)**. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.44 (3H, s, NCH_3); 3.08 ($2H_{ax}$, d, ^2J = 12.3, $2CH_2N$); 3.21 ($2H_{eq}$, d, ^2J = 12.3, $2CH_2N$); 3.32 (2H, br. s, CH_2); 3.86 (6H, s, $2OCH_3$). ^{13}C NMR spectrum, δ, ppm: 33.5 (CH_2); 45.2 (NCH_3); 54.2 (OCH_3); 58.5 (CH_2N); 89.3 (CNO_2); 164.9 (CO_2).

1,3-Diisopropyl-5-methoxycarbonyl-5-nitrohexahydropyrimidine (8) and 5-Hydroxymethyl-1,3-diisopropyl-5-nitrohexahydropyrimidine (9). From methyl nitroacetate **1** (1.0 g, 8.4 mmol), aqueous formalin (35%, 6.55 ml, 84 mmol), and diisopropylamine (3.63 ml, 42 mmol) to give compound **8** (0.81 g, 35.3%) and compound **9** (0.36 g, 17.5%) as a yellow-colored oil.

1,3-Diisopropyl-5-methoxycarbonyl-5-nitrohexahydropyrimidine (8). IR spectrum, ν, cm^{-1}: 1368, 1384 (*gem*-dimethyl group doublet); 1368, 1552 (NO_2); 1176, 1752 (CO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.02 and 1.07 (12H, two d, ^3J = 6.6, $4CH_3$); 2.87 (2H, sept, ^2J = 6.6, 2CH); 2.93 ($2H_{ax}$, d, ^2J = 12.0, $2CH_2N$); 3.16 ($1H_{ax}$, d, ^2J = 8.7, NCH_2N); 3.53 ($1H_{eq}$, d, ^2J = 8.7, NCH_2N); 3.62 ($2H_{eq}$, d, ^2J = 12.0, $2CH_2N$); 3.78 (3H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 17.54 and 18.91 (both CH_3); 50.68 (CH_2N); 52.38 (OCH_3); 53.50 (CHN); 70.30 (NCH_2N); 89.60 (CNO_2); 165.36 (CO_2). Mass spectrum, *m/z*: 273 $[M]^+$. Found, %: C 52.69; H 8.48; N 15.37. $C_{12}H_{23}N_3O_4$. Calculated, %: C 52.73; H 8.48; N 15.37.

5-Hydroxymethyl-1,3-diisopropyl-5-nitrohexahydropyrimidine (9). IR spectrum, ν, cm^{-1}: 1168 (*gem* dimethyl group doublet); 1364, 1568 (NO_2); 3264 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 and 1.09 (12H, two d, ^3J = 6.6, $4CH_3$); 2.79 ($2H_{ax}$, d, ^2J = 12.0, $2CH_2N$); 2.88 (2H, sept, ^2J = 6.6, 2CH); 3.27 ($2H_{eq}$, d, ^2J = 12.0, $2CH_2N$); 3.32 ($1H_{ax}$, d, ^2J = 8.7, NCH_2N); 3.39 ($1H_{eq}$, d, ^2J = 8.7, NCH_2N); 4.00 (2H, s, $C\underline{H_2}OH$); 4.12 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 17.73 and 18.87 (both CH_3); 50.37 (CH_2N); 52.55 (CHN); 66.00 (CH_2OH); 70.62 (NCH_2N); 88.65 (CNO_2). Mass spectrum, *m/z*: 245 $[M]^+$. Found, %: C 53.84; H 9.46; N 17.15. $C_{11}H_{23}N_3O_3$. Calculated, %: C 53.86; H 9.45; N 17.13.

1,3-Dibenzyl-5-methoxycarbonyl-5-nitrohexahydropyrimidine (11), 1-Benzyl-*cis*-3,5-bis(methoxycarbonyl)- (12a) and 1-Benzyl-*trans*-3,5-bis(methoxycarbonyl)-3,5-dinitropiperidine (12b). From methyl nitroacetate **1** (1.0 g, 8.4 mmol), aqueous formalin (35%, 6.55 ml, 84 mmol), and benzylamine (4.6 ml, 42 mmol) to give compound **11** (1.02 g, 33%) and compounds **12a,b** (0.04 g, 2.5%) as a yellow-colored oil.

1,3-Dibenzyl-5-methoxycarbonyl-5-nitrohexahydropyrimidine (11). IR spectrum, ν, cm^{-1}: 1360, 1552 (NO_2); 1264, 1748 (CO_2); 704, 752, 1456, 3032, 3048, 3064 (C_6H_5). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.04 ($2H_{ax}$, d, ^2J = 12.8, $2CH_2N$); 3.07 ($1H_{ax}$, d, ^2J = 9.9, NCH_2N); 3.53 ($1H_{eq}$, d, ^2J = 9.9, NCH_2N); 3.59 and 3.67 (4H, two d, ^2J = 13.4, $2PhCH_2N$); 3.75 (3H, s, OCH_3); 3.78 ($2H_{eq}$, d, ^2J = 12.8, CH_2N); 7.18-7.45 (10H, m, 2Ar). ^{13}C NMR spectrum, δ, ppm: 53.57 (OCH_3); 55.50 and 58.40 (CH_2N); 72.58 (NCH_2N); 89.00 (CNO_2); 127.24 (*p*-C_{Ph}); 128.18 and 128.68 (*o*- and *m*-C_{Ph}); 137.03 (*i*-C_{Ph}); 165.15 (CO_2). Mass spectrum, *m/z*: 369 $[M]^+$. Found, %: C 65.05; H 6.25; N 11.38. $C_{20}H_{23}N_3O_4$. Calculated, %: C 65.03; H 6.28; N 11.37.

1-Benzyl-*cis*-3,5-bis(methoxycarbonyl)- (12a) and 1-Benzyl-*trans*-3,5-bis(methoxycarbonyl)-3,5-dinitropiperidine (12b). IR spectrum, ν, cm^{-1}: 1340, 1550 (NO_2); 1250, 1760 (CO_2); 710, 750, 1450, 1490 (C_6H_5). ^{1}H NMR spectrum, δ, ppm (*J*, Hz) **12a**: 2.91 ($2H_{ax}$, d, ^2J = 12.7, CH_2N); 3.19 ($1H_{AB}$, d, ^2J = 15.9, CH_2); 3.55 ($2H_{eq}$, d, ^2J = 12.7, $2CH_2N$); 3.61 ($1H_{AB}$, d, ^2J = 15.9, CH_2); 3.68-3.76 (2H, m, $C_6H_5CH_2N$); 3.79 (6H, s, $2OCH_3$); 7.16-7.45 (5H, m, Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz) **12b**: 3.19 ($1H_{AB}$, d, ^2J = 15.5, $2CH_2N$); 3.29 ($2H_{AB}$, d, ^{2}J = 12.5 CH_2N); 3.35 (2H, br. s, CH_2); 3.68-3.76 (2H, m, $C_6H_5CH_2N$); 3.81 (6H, s, $2OCH_3$); 7.16-7.45 (5H, m, Ar). ^{13}C NMR spectrum, δ, ppm, **12a**: 54.10 (OCH_3); 56.00 (CH_2N); 58.55 ($C_{Ph}CH_2N$); 88.80 (CNO_2); 165.10 (CO_2). ^{13}C NMR spectrum, δ, ppm, **12b**: 34.10 (CH_2); 54.00 (OCH_3); 56.29 (CH_2N); 58.73 ($C_{Ph}CH_2N$); 89.22 (CNO_2); 127.95; 128.42; 129.09, 129.20, 129.33 and 135.45 (C_{Ph}); 164.88 (CO_2). Mass spectrum, *m/z*: 381 $[M]^+$. Found, %: C 50.41; H 5.05; N 10.99. $C_{16}H_{19}N_3O_8$. Calculated, %: C 50.39; H 5.02; N 11.02.

5-Methoxycarbonylmethyl-1,3-dimethyl-5-nitrohexahydropyrimidine (13) and 5-methoxycarbonylmethylidene-1,3-dimethylhexahydropyrimidine (14). From methyl 3-nitropropionate **2**, (0.5 g, 3.76 mmol), aqueous formalin (35%, 2.93 ml, 37.6 mmol), and aqueous methylamine (25.2%, 2.31 g, 18.8 mmol) to give compound **13** (0.42 g, ~ 47%) and compound **14** (0.36 g, ~ 51%). Lowering the reaction temperature to 20ºC leads to an increase in the yield of the hexahydropyrimidine **13** to 70% and the yield lowering of compound **14** to 29%.

5-Methoxycarbonylmethyl-1,3-dimethyl-5-nitrohexahydropyrimidine (13). IR spectrum, ν, cm^{-1}: 1160, 1740 (CO_2); 1370, 1550 (NO_2); 2780 (CH_3N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.24 (6H, s, $2CH_3N$); 2.79 ($1H_{ax}$, d, ^2J = 8.6, NCH_2N); 2.87-2.94 (5H, $1H_{eq}$, m, NCH_2N, 4H, $2CH_2N$); 3.14 (2H, s, CH_2CO_2); 3.63 (3H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 14.2 (CH_3); 35.0 (CH); 33.7 ($\underline{C}H_2CO_2$); 46.4 (NCH_3); 51.9 (OCH_3); 59.5 (CH_2N); 78.5 (NCH_2N); 84.4 (CNO_2), 169.2 (CO_2). Mass spectrum, *m/z*: 231 $[M]^+$. Found, %: C 46.52; H 7.41; N 18.17. $C_9H_{17}N_3O_4$. Calculated, %: C 46.74; H 7.41; N 18.17.

5-Methoxycarbonylmethylidene-1,3-dimethylhexahydropyrimidine (14). IR spectrum, ν, cm^{-1}: 840 (C=CH); 1160, 1720 (CO_2); 2770 (CH_3CN). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.25 and 2.29 (6H, two s, $2CH_3N$); 3.03 and 3.27 (4H, two s, $2CH_2CN$); 3.65 (3H, s, OCH_3); 3.7 (2H, s, NCH_2N); 5.71 (1H, s, C=CH). ^{13}C NMR spectrum, δ, ppm: 41.8 and 41.9 (NCH_3); 51.0 (OCH_3); 53.46 and 60.9 (CH_2N); 77.0 (NCH_2N); 115.9 (C=$\underline{C}$H); 151.4 ($\underline{C}$=CH); 166.2 (CO_2). Mass spectrum, *m/z*: 184 $[M]^+$. Found, %: C 58.72; H 8.69; N 15.17. $C_9H_{16}N_2O_2$. Calculated, %: C 58.67; H 8.75; N 15.21.

5-Methoxycarbonylmethylidene-1,3-dimethylhexahydropyrimidine (14). A solution of **13** (0.5 g, 2.20 mmol) in Bu_2NH (5 ml, 29.68 mmol) was stirred for 4 h at 20ºC, dissolved in chloroform (10 ml), washed with water (3 x 10 ml), and dried over Na_2SO_4. The solvent was removed under reduced pressure to give compound **14** (0.39 g, 98%) as an oil.

This work was carried out with the financial support of the Basic Research Program of the Presidium of the Russian Academy of Sciences "Study of methods for preparing chemical materials and development of novel materials"

REFERENCES

1. H. H. Baer and L. Urbas, in: H. Feuer (editor), *The Chemistry of the Nitro and Nitroso Groups* [Russian *trans*lation], Vol. 2, Mir, Moscow (1973), p. 63.
2. S. S. Novikov, G. A. Shvekhgeimer, V. V. Sevastyanova, and V. A. Shlyapochnikov, *The Chemistry of Aliphatic and Alicyclic Nitro Compounds* [in Russian], Khimiya, Moscow (1974), pp. 41, 266.
3. R. Jeyaraman and S. Avila. *Chem. Rev.*, **81**, 149 (1981).
4. L. Vijayalakshmi, V. Parthasarathi, M. Venkatraj, and R. Jeyaraman, *Acta Crystallogr.*, **C56**, 1240 (2000).
5. Yu. M. Atroshchenko, E. G. Nikiforova, I. V. Shakhkeldyan, Yu. D. Grudtsyn, N. G. Akhmedov, E. N. Alifanova, O. Ya. Borbulevich, O. V. Shishkin, S. S. Gittis, and A. Ya. Kaminskii, *Zh. Obshch. Khim.*, **36**, 771 (2000).
6. N. N. Yarmukhamedov, N. Z. Baibulatova, T. V. Khakimova, L. V. Spirikhin, V. A. Dokichev, and M. S. Yunusov, *Izv. Akad. Nauk, Ser. Khim.*, 255 (2001).
7. R. G. Kostyanovsky, K. A. Lyssenko, I. A. Bronzova, O. N. Krutius, Y. A. Strelenko, and A. A. Korlyukov, *Mendeleev Commun.*, 106 (2000).
8. N. S. Zefirov, V. A. Palyulin, G. A. Efimov, O. A. Subbotin, O. I. Levina, K. A. Potekhin, and Yu. T. Struchkov, *Dokl. Akad. Nauk.*, **320**, 1392 (1991).

9. G. L. Arutyunyan, A. A. Chachoyan, V. A. Shkulev, G. G. Adamyan, Ts. E. Agadzhanyan, and B. T. Garibdzhanyan, *Khim. –Farm. Zh.*, **29**, No. 3, 33 (1995).
10. L. Virag, T. Fazekas, N. Iost, A. Varro, K. D. Berlin, B. J. Scherlag, R. Lazzara, and J. G. Papp, *Life Sci. /Pharmacol. Lett;*, **66**, 253 (2000).
11. A. Björ, M. Björsne, T. Halvarsson, K.-J. Hoffmann, B. Samuelsson, and G. Strandlund, US Pat. 6887881; *Chem. Abstr*, **134**, 42151 (2001).
12. N. N. Yarmukhamedov, N. Z. Baibulatova, V. A. Dokichev, Yu. V. Tomilov, and M. S. Yunusov, *Izv. Akad. Nauk, Ser. Khim.*, 721 (2001).
13. N. N. Yarmukhamedov, N. Z. Baibulatova, V. A. Dokichev, T. V. Khakimova, L. V. Spirikhin, Yu. V. Tomilov, and M. S. Yunusov, *Izv. Akad. Nauk, Ser. Khim.*, 405 (2005).
14. L. I. Vlasova, N. Z. Baibulatova, L. D. Latypova, M. S. Yunusov, V. A. Dokichev, and Yu. V. Tomilov, *Izv. Akad. Nauk, Ser. Khim.*, 469 (2005).
15. R. R. Shakirov, L. I. Vlasova, D. V. Shishkin, N. N. Yarmukhamedov, N. Z. Baibulatova, D. G. Semesko, V. A. Dokichev, and Yu. V. Tomilov, *Izv. Akad. Nauk, Ser. Khim.*, 1687 (2005).
16. M. D. Mashkovskii, *Drugs* [in Russian], Vol. 1, Torsing, Kharkiv (1998), p. 370.
17. V. G. Granik and N. B. Grigorev, *Izv. Akad. Nauk, Ser. Khim.*, 1819 (2002).
18. R. R. Shakirov, N. N. Yarmukhamedov, L. I. Vlasova, N. Z. Baibulatova, R. Yu. Khisamutdinova, S. F. Gabdrakhmanova, L. T. Karachurina, and N. Zh. Baschenko, *Khim.-Farm. Zh.*, **40**, No. 1, 29 (2006).
19. G. M. Blackburn, I. G. Beadham, H. Adams, A. P. Hutchinson and S. Nicklin, *J. Chem. Soc., Perkin Trans. 1*, 225 (2000).
20. H. Piotrowska, T. Urbanski and I. Wolochowicz, *Bull. Pol. Acad. Sci., Ser. Sci. Chim.*, **19**, 591 (1971).
21. P. Noble Jr., F. G. Borgardt, and W. L. Reed, *Chem. Rev.*, **64**, 19 (1964).
22. G. A. Shvekhgeimer, N. F. Pyatakov, and S. S. Novikov, *Usp. Khim.*, **28**, 484 (1959).
23. V. I. Isagulgants and E. L. Markosyan, *Nafta Zagreb*, **17**, 217 (1966); *Chem. Abstr.*, **67**, 108164 (1967).
24. S. Zen, M. Koyama, and S. Koto, *Org. Synth.*, **55**, 77 (1976).
25. V. M. Belikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 855 (1956).