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# Synthesis and Structure of *N*-Methyl-1-[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]fullerene-$C_{60}$-[1,9-*c*]pyrrolidine

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**Abstract**—Three-component condensation of fullerene $C_{60}$ with sarcosine and 4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde under the conditions of the Prato reaction has afforded new fulleropyrrolidine; the product structure has been confirmed by IR and NMR spectroscopy as well as mass spectrometry.

**Keywords**: fullerene functionalization, fullerene $C_{60}$, fulleropyrrolidine, the Prato reaction

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Fullerenes and their derivatives possess a range of valuable physical, photo- and electrochemical properties leading to a variety of potential medical applications. Fullerenes as such are extremely hydrophobic and therefore are hardly suitable for administration to a living organism. However, the recently developed methods of fullerenes chemical modifications using water-soluble and lipophilic adducts have allowed preparation of the derivatives revealing various biological effects [1]: absorption of free radicals and protection from oxidative stress [2], transfer of HIV proteases [3], and generation of singlet oxygen causing damage of DNA of the transformed (tumor) cells [4]. Certain organic derivatives of fullerenes are capable of penetration through lipid membranes, overcoming hematoencephalic barrier, and modulation of ions transport [5]. Lipophilic and membranotropic properties of fullerene $C_{60}$ are essentially important for development of drugs efficient against pathogenic agents.

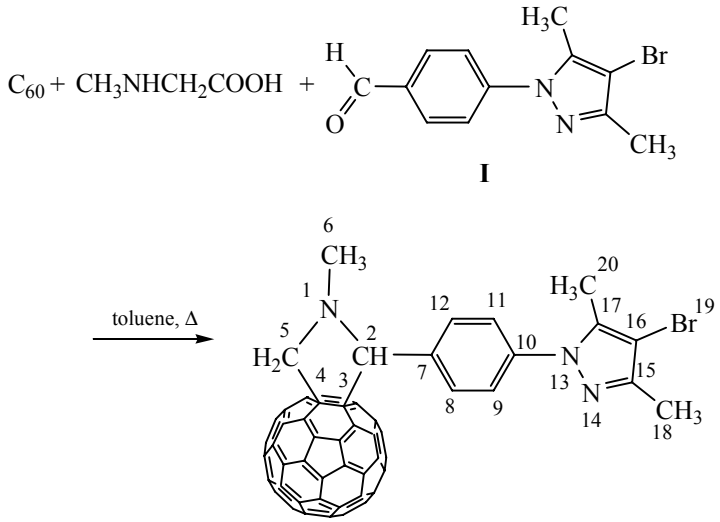
Functionalizing of fullerene sphere based on the Prato reaction [6] has recently become a leading method in targeted synthesis of new materials and bioactive compounds. Accessibility of various aldehydes has allowed preparation of a series of dimeric and trimeric donor–acceptor dyes and investigation of their photophysical and biological properties [5, 7]. *N*-Methyl-1-(4-aminophenyl)fullero-$C_{60}$-[1,9-*c*]pyrrolidines based on novel 4-*N*-aminobenzaldehydes (4-morpholyl- and 4-piperidiylbenzaldehyde) have been described earlier in [8].

Herein we describe preparation and structure elucidation of another fulleropyrrolidine, *N*-methyl-1-[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]fullero-$C_{60}$-[1,9-*c*]pyrrolidine, starting from 4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde **I** [9].

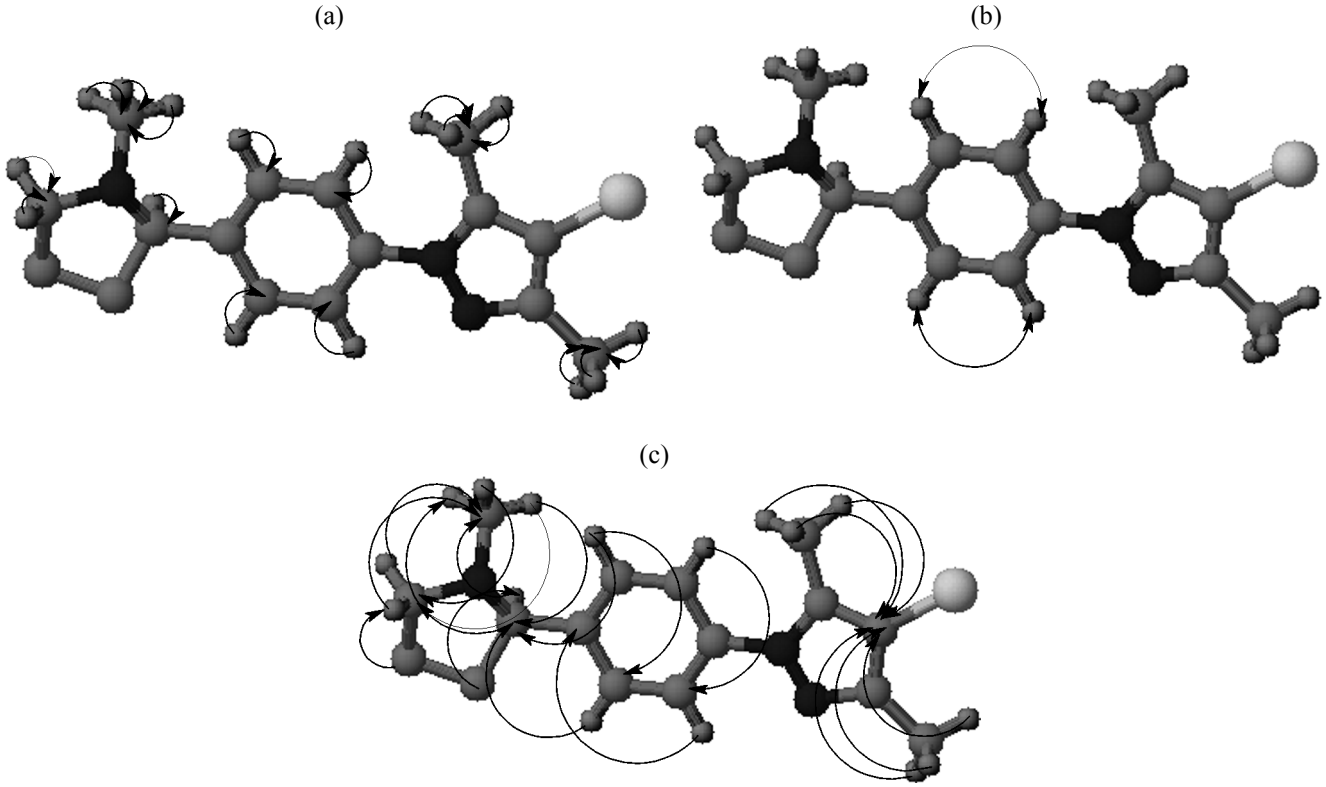
Three-component condensation of fullerene $C_{60}$, *N*-methylglycine (sarcosine), and 4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde was performed under the conditions of Prato reaction in toluene upon heating during 4–5 h. After the reaction was complete, the unreacted starting compound and the reaction product **II** were separated by means of column chromatography on $SiO_2$ eluting sequentially with toluene and pyridine. The unreacted fullerene was eluted first; yield of the target fulleropyrrolidine **II** was of 88% (Scheme 1).

Mechanism of fulleropyrrolidine **II** formation likely included 1,3-dipolar addition to fullerene $C_{60}$ through the intermediate formation of active azomethynilides [6]. Condensation of the aromatic aldehyde with

**Scheme 1.**




sarcosine via nucleophilic addition of the amino group of sarcosine at the carbonyl group of aldehyde **I** was the first reaction stage. The formed adduct further eliminated a water molecule and then underwent decarboxylation to form azo-ylide, the latter acting as a nucleophile attacking the fullerene core at the 6–6 double bond to close the pyrrolidine ring. Structure of the prepared compound **II** was elucidated using data of IR, $^{1}$H and $^{13}$C NMR (COSY, HSQC, and HMBC experiments) as well as mass spectrometry.




Scheme of the correlations in HSQC (a), COSY (b), and HMBC (c) spectra of compound **II**.

IR spectrum of compound **II** contained absorption bands of pyridine ring C–N bonds, the fullerene fragment, and C–H and N–H bonds.

$^1$H NMR spectrum of compound **II** contained singlet signals of the methyl group protons at 2.30–2.86 ppm. The signals at 4.32–4.34 and 5.03–5.05 ppm were assigned to protons of the tertiary ($C^2$) and secondary ($C^5$) atoms of the saturated heterocycle, respectively. Equivalent protons of the aromatic fragment resonated in weak field at 7.51–7.67 and 7.96–8.02 ppm.

$^{13}$C NMR spectrum of compound **II** contained the methyl group signals at 12.07 ($C^{20}$), 12.43 ($C^{18}$), and 40.06 ($C^6$) ppm. The methylene and methine carbon atoms of the saturated aza-heterocycle resonated at 69.88 and 68.92 ppm, respectively. Signals of the aromatic fragment appeared in weak field at 123.91–124.50 and 130.19–130.72 ppm. The quaternary $C^3$ and $C^4$ atoms resonated as singlet signals at 97.07 ppm.

Six correlations were observed in the HSQC $^1$H–$^{13}$C spectrum, indicating the spin-spin coupling between the following pairs of atoms: $H^{18}$ and $C^{18}$, $H^{20}$ and $C^{20}$, $H^6$ and $C^6$, $H^2$ and $C^2$, $H^5$ and $C^5$, $H^9$ and $C^9$, $H^{11}$ and $C^{11}$, $H^8$ and $C^8$, $H^{12}$ and $C^{12}$ (see figure).

Molecular ion peak with *m*/*z* 1027.021 was detected in mass spectrum of compound **II**.

The prepared *N*-methyl-1-[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]fullero-$C_{60}$-[1,9-*c*]pyrrolidine **II** is of interest not as a biologically active compound as well as for organic photovoltaics applications [6] due to the presence of fullerene sphere, pyrrolidine ring, and pyrazole fragment in the structure.

## EXPERIMENTAL

IR spectrum was recorded with an AVATAR-320 Nicolet Fourier spectrometer (KBr pellets). $^1$H and $^{13}$C NMR spectra were registered using a Bruker Avance-400 (500 MHz) spectrometer (solution in $CDCl_3$–$CS_2$ 1 : 5 with TMS as internal reference). Mass spectrum was obtained with a MALDI TOF/TOF Autoflex-III Bruker instrument. TLC analysis was performed on a Sorbfil plates developed with iodine vapor.

Fullerene $C_{60}$ (99.5% purity) was purchased from NeoTekProduct (Saint Petersburg).

***N*-Methyl-1-[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]fullero-$C_{60}$-[1,9-*c*]pyrrolidine (II)**. A mixture of a solution of 40 mg (0.0555 mmol) of $C_{60}$ in 40 mL of toluene, 80 mg (0.0275 mmol) of 4-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)benzaldehyde, and 9.8 mg (0.1112 mmol) of *N*-methylglycine was heated under reflux during 4 h. After the solvent removal, the residue was purified via column chromatography on silica gel eluting first with toluene to remove unreacted $C_{60}$ and then with pyridine to isolate the fulleropyrrolidine **II**. Yield 24.6 mg (88%). $^1$H NMR spectrum, δ, ppm: 2.33 s (3H, $CH_3$), 2.30 s (3H, $CH_3$), 2.86 s (3H, $CH_3$), 7.51 d (1H, $CH^9_{arom}$, $J_{HH}$ 6.8 Hz), 7.67 d (1H, $CH^{11}_{arom}$, $J_{HH}$ 6.4 Hz), 7.95 d (1H, $CH^8_{arom}$, $J_{HH}$ 6.8 Hz), 8.01 d (1H, $CH^{12}_{arom}$, $J_{HH}$ 6.4 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 135.53–156.09 (58C, fullerene), 154.71 ($C^{12}$), 131.43 ($C^{10}$), 129.96 ($C^8$), 127.77 ($C^9$), 115.18 ($C^{11}$), 113.34 ($C^7$), 83.03 ($C^{16}$), 69.77 ($C^{15}$), 68.66 ($C^{14}$), 66.22 ($C^5$), 66.29 ($C^4$), 48.79 ($C^2$), 47.32 ($C^4$), 39.79 ($C^{18}$), 29.83 ($C^{13}$). Mass spectrum, *m*/*z* ($I_{rel.}$, %): 1027.021 $[M]^+$ (calculated for $C_{74}H_{22}BrN_3$: 1026.095).

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